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(54) Title: HUMAN CANCER ASSOCIATED GENE SEQUENCES AND POLYPEPTIDES

(57) Abstract

This invention relates to newly identified tissue specific cancer associated polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "cancer antigens", and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such tissue specific cancer antigens for detection, prevention and treatment of tissue specific disorders, particularly the presence of cancer. This invention relates to the cancer antigens as well as vectors, host cells, antibodies directed to cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing tissue specific disorders, including cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.

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Human Cancer Associated Gene Sequences and Polypeptides

5 Field of the Invention

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This invention relates to newly identified tissue specific cancer associated polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "cancer antigens," and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such cancer antigens for detection, prevention and treatment of tissue specific diseases, particularly cancers. This invention relates to the cancer antigens as well as vectors, host cells, antibodies directed to cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to tissue specific diseases, including cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.

20 Background of the Invention

Cell growth is a carefully regulated process which responds to specific needs of the body. Occassionally, the intricate, and highly regulated controls dictating the rules for cellular division break down. When this occurs, the cell begins to grow and divide independently of its homeostatic regulation resulting in a condition commonly referred to as cancer. In fact, cancer is the second leading cause of death among Americans aged 25-44.

Cancers or malignant tumors are characterized by continuous cell proliferation and cell death. Cancer cells have been shown to exhibit unique gene expression, and dozens of cancer-specific genetic markers, tumor antigens, have been identified. P35B, a tumor rejection antigen, was first identified in mouse. A point mutation in the P35B gene elicits a cytolytic T lymphocyte response but no detectable antibody response (Szikora, J. P. et al. (1990) EMBO J. 9:1041-1050). A human homolog of P35B, FX, is a homodimeric

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NADP(H)-binding protein of 68 kDa. FX acts as a combined epimerase and NADPH-dependent reductase in converting GDP-4-keto-6-D-deoxymannose to GDP-L-fucose (Tonetti, M. et al. (1996) J. Biol. Chem. 271: 27274-27279). GDP-L-fucose is the substrate of several facosyl-transferases involved in the biosysthesis of blood group ABH antigenic determinants. GDP-L-fucose is also utilized in synthesizing fucosylated glycoproteins and glycolipids which function in cell adhesion and recognition (Springer, T. A. and Lasky, L. A. (1991) Nature 329: 196-197; Brandley, B. K. et al. (1990) Cell 63: 861-863; and Feizi, T. and Childs, R. A. (1987) Biochem. J. 245: 1-11).

Thus, there is a need for the identification and characterization of novel tissue specific polynucleotides and polypeptides which modulate activation and differentiation of cells, both normally and in disease states. In particular, there is a need to isolate and characterize additional molecules that mediate apoptosis, DNA repair, tumor-mediated angiogenesis, genetic imprinting, immune responses to tumors and tumor antigens and, among other things, that can play a role in detecting, preventing, ameliorating or correcting dysfunctions or diseases.

Summary of the Invention

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The present invention includes isolated nucleic acid molecules comprising, or alternatively, consisting of, a cancer associated polynucleotide sequence disclosed in the sequence listing (as SEQ ID NOs:1 to 842) and/or contained in a human cDNA clone described in Tables 1, 2 and 5 and deposited with the American Type Culture Collection ("ATCC"). Fragments, variant, and derivatives of these nucleic acid molecules are also encompassed by the invention. The present invention also includes isolated nucleic acid molecules comprising, or alternatively consisting of, a polynucleotide encoding a cancer polypeptide. The present invention further includes cancer polypeptides encoded by these polynucleotides. Further provided for are amino acid sequences comprising, or alternatively consisting of, cancer polypeptides as disclosed in the sequence listing (as SEQ ID Nos: 843 to 1684) and/or encoded by a human cDNA clone described in Tables 1, 2 and 5 and deposited with the ATCC. Antibodies that bind these polypeptides are also encompassed by the invention. Polypeptide fragments, variants, and derivatives of these amino acid sequences are also encompassed by the invention, as are polynucleotides encoding these polypeptides and antibodies that bind these polypeptides. Also provided are diagnostic methods for diagnosing

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and treating, preventing, and/or prognosing disorders related to cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of cancer antigens of the invention.

Detailed Description

Tables

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Table I summarizes some of the cancer antigens encompassed by the invention (including contig sequences (SEQ ID NO:X) and the cDNA clone related to the contig sequence) and further summarizes certain characteristics of the cancer polynucleotides and the polypeptides encoded thereby. The first column shows the "SEQ ID NO:" for each of the 842 cancer antigen polynucleotide sequences of the invention. The second column provides a unique "Sequence/Contig ID" identification for each cancer associated sequence. The third column, "Gene Name," and the fourth column, "Overlap," provide a putative identification of the gene based on the sequence similarity of its translation product to an amino acid sequence found in a publicly accessible gene database and the database accession no. for the database sequence having similarity, respectively. The fifth and sixth columns provide the location (nucleotide position nos. within the contig), "Start" and "End", in the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred ORF shown in the sequence listing as SEQ ID NO:Y. The seventh and eighth columns provide the "% Identity" (percent identity) and "% Similarity" (percent similarity), respectively, observed between the aligned sequence segments of the translation product of SEQ ID NO:X and the database sequence. The ninth column provides a unique "Clone ID" for a cDNA clone related to each contig sequence. The tenth column shows the tissue in which each SEQ ID NO:X is predominantly expressed.

Table 2 summarizes ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application.

Table 3 indicates public ESTs, of which at least one, two, three, four, five, ten, fifteen or more of any one or more of these public EST sequences are optionally excluded from certain embodiments of the invention.

Table 4 lists residues comprising antigenic epitopes of antigenic epitope-bearing fragments present in most of the cancer associated polynucleotides described in Table 1 as predicted by the inventors using the algorithm of Jameson and Wolf, (1988) Comp. Appl.

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Biosci. 4:181-186. The Jameson-Wolf antigenic analysis was performed using the computer program PROTEAN (Version 3.11 for the Power MacIntosh, DNASTAR, Inc., 1228 South Park Street Madison, WI). Cancer associated polypeptides (e.g., SEQ ID NO:Y, polypeptides encoded by SEQ ID NO:X, or polypeptides encoded by the cDNA in the referenced cDNA clone) may possess one or more antigenic epitopes comprising residues described in Table 4. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. The residues and locations shown in column two of Table 4 correspond to the amino acid sequences for most cancer associated polypeptide sequence shown in the Sequence Listing.

Table 5 shows the cDNA libraries sequenced, and ATCC designation numbers and vector information relating to these cDNA libraries.

Definitions

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The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X (as described in column 1 of Table 1) or the related cDNA clone (as described in column 9 of Table 1 and contained within a library deposited with the ATCC). For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence.

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Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

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In the present invention, "SEQ ID NO:X" was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X is deposited at Human Genome Sciences, Inc. (HGS) in a catalogued and archived library. As shown in column 9 of Table 1, each clone is identified by a cDNA Clone ID. Each Clone ID is unique to an individual clone and the Clone ID is all the information needed to retrieve a given clone from the HGS library. In addition to the individual cDNA clone deposits, most of the cDNA libraries from which the clones were derived were deposited at the American Type Culture Collection (hereinafter "ATCC"). Table 5 provides a list of the deposited cDNA libraries. One can use the Clone ID to determine the library source by reference to Tables 2 and 5. Table 5 lists the deposited cDNA libraries by name and links each library to an ATCC Deposit. Library names contain four characters, for example, "HTWE." The name of a cDNA clone ("Clone ID") isolated from that library begins with the same four characters, for example "HTWEP07". As mentioned below, Table 1 correlates the Clone ID names with SEQ ID NOs. Thus, starting with a SEQ ID NO, one can use Tables 1, 2 and 5 to determine the corresponding Clone ID, from which library it came and in which ATCC deposit the library is contained. Furthermore, it is possible to retrieve a given cDNA clone from the source library by techniques known in the art and described elsewhere herein. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposits were made persuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, or the complement thereof (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein), and/or sequences contained in the related cDNA clone within a library deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH

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7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

Also included within "polynucleotides" of the present invention are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

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Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

The polynucleotides of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the

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polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

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In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

"SEQ ID NO:X" refers to a tissue specific cancer antigen polynucleotide sequence described in Table 1. SEQ ID NO:X is identified by an integer specified in column 1 of Table 1. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO:X. There are 842 cancer antigen polynucleotide sequences described in Table 1 and shown in the sequence listing (SEQ ID NO:1 through SEQ ID NO:842). Likewise there are 842 polypeptide sequences shown in the sequence listing, one polypeptide sequence for each of the polynucleotide sequences (SEQ ID NO:843 through SEQ ID NO:1684). The polynucleotide sequences are shown in the sequence listing immediately followed by all of the polypeptide sequences. Thus, a polypeptide sequence corresponding to polynucleotide sequence SEQ ID NO:1 is the first polypeptide sequence shown in the sequence listing. The second polypeptide sequence corresponds to the polynucleotide sequence shown as SEQ ID NO:2, and so on. In otherwords, since there are842 polynucleotide sequences, for any polynucleotide sequence SEQ ID NO:X, a corresponding polypeptide SEQ ID NO:Y can be determined by the formula X + 842 = Y. In addition, any of the unique "Sequence/Contig ID" defined in column 2 of Table 1, can be linked to the corresponding polypeptide SEQ ID NO:Y by reference to Table 4.

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The polypeptides of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees 10 at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

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The cancer polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

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The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The cancer polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

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By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

"A polypeptide having functional activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular assay, such as, for example, a biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).

The functional activity of the cancer antigen polypeptides, and fragments, variants derivatives, and analogs thereof, can be assayed by various methods.

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For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the present invention for binding to an antibody to the full length polypeptide antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

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In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky, E., et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, physiological correlates polypeptide of the present invention binding to its substrates (signal transduction) can be assayed.

In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants derivatives and analogs thereof to elicit polypeptide related biological activity (either in vitro or in vivo). Other methods will be known to the skilled artisan and are within the scope of the invention.

Cancer Associated Polynucleotides and Polypeptides of the Invention

It has been discovered herein that the polynucleotides described in Table 1 are expressed at significantly enhanced levels in human cancer tissues as shown in column 10 of

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Table 1. Accordingly, such polynucleotides, polypeptides encoded by such polynucleotides, and antibodies specific for such polypeptides find use in the prediction, diagnosis, prevention and treatment of tissue specific disorders, including cancer as more fully described below.

Table 1 summarizes some of the polynucleotides encompassed by the invention (including contig sequences (SEQ ID NO:X) and the related cDNA clones) and further summarizes certain characteristics of these tissue specific cancer associated polynucleotides and the polypeptides encoded thereby.

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Seq ID Contig ID No. 507291	Gene Name uvomorulin [Homo sapiens] >sp[Q15855[Q15855	Overlap gil340185	HGS N Start	HGS Nucleotide % Start End % Ider	tide % % Identity Similarity	% imilarity 100	Clone ID	Tissue(s)
208000	(ARC-I/UVOMORULIN) > gil930046 uvonnorulin (140 AA) [Homo sapiens] [5UB 168-307] Length = 878 HLA-B-associated transcript 2 (BAT2) [Homo sapiens] > girl179345 HLA-B-associated transcript 2 (BAT2) [Homo sapiens] > pirlB35098[B35098 MHC class III histocompatibility antigen HLA-B-	8il 79339	001	1902	9		HWAAK56	Lung. Breast/Ovirian
518325	associated transcript 2 - human >splP48634 BAT2_HUMAN LARGE PROLINE- RICH P		011	310			HHFCP36	Lung, Panereas.
523111	Sm D2 [Homo sapiens] >pir[138861 138861 small nuclear ribonucleoprotein chain D2 - human Length = 118	gi 600748	233	029	œ *	88	HATAE67	Breast/Ovarian Lung. Breast/Ovarian
526869	(AC002291) Similar ATP-dependent RNA Helicase [Arabidopsis thaliana] >sp 049289 049289 SIMILAR ATP-DEPENDENT RNA HELICASE. Length = 845	gi 2829912	-	552	6 9	<i>E</i> .	HT4IP57	Panereus. Breust/Ovarian
532211	retinuic acid-binding protein [Bos taurus] Length = 138	gi 162906	6	481	95	86	HHGCV63	Lung. Breast/Ovarian

Pancreas.	breast/Ovarian Lung. Breast/Ovarian	Lung.	Lung, Pancreas	Lung, Panewas	Lung. Pancreas. Breast/Ovarian
HEBCC47	HUSIB86	HRGBU25	111/11/17/27	HTDAEI0	ннесх90
	92		92	16	001
•	92		92	16	001
384	1149	635	1189	931	8 41
091	-	174	C1	79	10
	gi 178130	·	gil1297297	gi 1030053	gi 28583
	alcohol dehydrogenase [Homo sapiens] >gi 178134 alcohol dehydrogenase 3 [Homo sapiens] >pirJH0789 DEHUCZ alcohol dehydrogenase (EC 1.1.1.1) 5 - human >sp P11766 ADHX_HUMAN ALCOHOL DEHYDROGENASE CLASS III CHI CHAIN (EC 1.1.1.1) (GLUTATHIONE- DEPENDENT FOR		transketolase [Homo sapiens] Length = 623	rtvp-1 [Homo sapiens] >pit/JC5308/JC5308 testisspecific, vespid, and pathogenesis-related protein 1 - human >splP48060/GLIP_HUMAN GLIOMA PATHOGENESIS-RELATED PROTEIN (RTVP-1 PROTEIN). Length = 266	delta- aminolevulinate synthase (housekeeping) [Homo sapiens] >pirfS13682 SYHUAL 5- aminolevulinate synthase (EC 2.3.1.37) I precursor - human >>plP13196 HEM1_HUMAN 5- AMINOLEVULINIC ACID SYNTHASE MITOCHONDRIAL PRECURSOR, NONSPECIFIC (EC 2.3.1.37) (DELTA-AM
532247	537932	540117	547710	551747	552799

						. •
HUKD144 Lung, Pancwas	Lung. Panereiss	Lung. Pancreas		Panereas. Breast/Ovarian	Pancreas.	Lung. Pancreas. Colon.
HUKD144	HADGE84	HUSGK19	HUPCN61	I COHIBMB 2	HBAMC47	HUKAL69
8	96		001	801		88
. 63	96		86	<u>.</u>		68
1017	459	776	429	623	522	965
202	-	e	-	219	367	m
gi 313002	gi]3288916		gi 567128	gni P1D c1294465		pidS10572 S10572
RING7 [Homo sapiens] >gi 557702 HLA-DMB [Homo sapiens] >gi 512472 HLA-DMB [Homo sapiens] >gi 104742 DMB [Homo sapiens] >pi 137533 137533 MHC class II histocompatibility antigen HI.A-DM beta chain precursor - human Length = 263	(AF053944) aortic carboxypeptidase-like protein ACLP [Homo sapiens] >splG3288916[G3288916 AORTIC CARBOXYPEPTIDASE-LIKE PROTEIN ACLP. >gnlPID[d1013781 AEBP1 [Homo sapiens] {SUB 314-1158} Length = 1158		immunoglobulin heavy chain [Homo sapiens] Length = 152	dJ68O2.2 [Homo sapiens] >spl735579 MYSN_HUMAN MYOSIN HEAVY CHAIN, NONMUSCLE TYPE A (CELLULAR MYOSIN HEAVY CHAIN, TYPE A) (NMMHC- A), >gi]553596 cellular myosin heavy chain [Homo sapiens] [SUB 1-1337]. Length = 1960	t	epithelial tumor antigen precursor, membranebound form - human Length = 515
553243	553368	554349	558491	558983	572943	585892
13	4	15	91	7	<u>∞</u>	<u>8</u>

						,
Lung. Pancreas	Lung, Panereas, Colon	Lung, Pancreas	Pancicas, Breast/Ovarian	Lung. Breast/Ovarian	Pancreas. Breast/Ovarian	Lung, Colon
HSRABIO	HMCEP91	HAJCB44	HEONC67	HDPPP20	HSSEH29	HDTDH46
. 96		70	97	66		100
96		29	76	66	•	100
983	1057	390	325	1652	1117	590
m	800	_	. 26	99	-	m
gniPID e222400		gi 1537068	gi 1815622	gniiPtD d1021210		gi 65780
C1 inhibitor [Homo sapiens] >gi[29535 C1 inhibitor [Homo sapiens] >pir[S15386 ITHUC1 complement C1 inhibitor precursor - human >splP05155 IC1_HUMAN PLASMA PROTEASE C1 INHIBITOR PRICURSOR (C1 INH) >gul [P11]e3783 C1 inhibitor (AA 155-478) (1 is 2nd base i		nucleoporin p58 [Rattus norvegicus] >sp P70581 P70581 NUCLEOPORIN P58. Length = 585	sclenophosphate synthetase 2 [Homo-sapiens] >splQ99611[Q99611 SELENOPHOSPHATE SYNTHETASE 2. Length = 448	karyopherin alhph 3 [Homo sapiens] >sp[000505 IMA3_HUMAN IMPORTIN ALPHA- 3 SUBUNIT (KARYOPHERIN ALPHA-3 SUBUNIT). Length = 521		ubiquitin conjugating-protein [Oryctolagus cuniculus] >gi 184046 HHR6B (Human homologue of yeast RAD 6); putative [Homo sapiens] >gi 30954 E2 protein [Homo sapiens] >gi 30954 E2 protein [Homo sapiens] >gil207355 ubiquitin conjugating-protein [Rattus norvegicus] >gn PtD e233515 HR6B gene pr
589390	596882	616289	622140	623566	647714	647752

631774 P58 [Homo sapiens] disulfide-isomerase (human >splP3010 le PROTEIN DISULFII PRECURSOR (EC 5 MICROSOMAL PRC (ERP57). Length	28 651995 collagen [Mus muscu collagen apha 1(VIII) > splQ00780[CA 18_N I(VIII) CHAIN PRE I-VIII collagen [rats, Partial, 172 aa] [Ratta	652156 phospholipid hydroperoxide glutathic [Homo sapiens] >sp 043381 043381 GSHH HUMAN (EC 1.11.1.9) (GLUP PEROXIDASE) >sp 3399677 (AC00 GSSH_HUMAN, partial CDS [Home {SUB 149-197} Length = 197	30 653010 31 655904 von Willebrand factor [Homo supiens]	32 657852	33 666414
P38 [Homo sapiens] >pirJS68363]S68363 protein disulfide-isomerase (EC 5.3.4.1) ER60 precursor-human >splp30101ER60_HUMAN PROBABLE PROTEIN DISULFIDE ISOMERASE ER-60 PRECURSOR (EC 5.3.4.1) (ERP60) (58 KD MICROSOMAL PROTEIN) (PS8) (GRPS8) (ERP57). Length	collagen [Mus musculus] >pirfS23779 S23779 collagen alpha I(VIII) chain - mouse >splQ00780 CA 18_MOUSE COLLAGEN ALPHA I(VIII) CHAIN PRECURSOR. >bbs 134935 alpha I-VIII collagen [rats, mesangial cell, Peptide Partial, 172 aa] [Rattus sp.] (SUB 399-570) Leng	phospholipid hydroperoxide glutathione peroxidase [Homo sapiens] >sp[043381]043381 GSHH HUMAN (EC 1.11.1.9) (GLUTATHIONE PEROXIDASE) >si[3399677 (AC005390) GSSH_HUMAN, partial CDS [Homo sapiens] {SUB 149-197} Length = 197	von Willebrand factor [Homo supiens] -pirlA34480[VWHU von Willebrand factor precursor - human -gi 553810 von Willebrand factor [Homo sapiens] {SUB 990-1947} -gn PID e222518 von Willebrand factor [Homo sapiens] {SUB 1-178} -gi 340316 von Willebrand antige	•	
gil 147739	gnijPIDjc245912	gil825667	Bij340356		
÷	n	262	632	92	-
1632	335	633	183	522	285
96	. 06	46	96		
96	95	46	96		
HDPAA15	HBTAD44	HOFBK80	HSRAA58 HSEBB94	HCHAL14	110SFG18
Lung, Pancreus. Breast/Ovarian	Lang, Panereas	Lung. Breast/Ovarian	Lung. Panereas Lung. Breast/Ovarian	Colon.	Lung, Panereas

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	rioosomai protein S9 (kattus norvegicus) >pirlJN0587JS21497 ribosomal protein S9 - rat Length = 194	gi 57.143	-	<u> </u>	86	86	HCF:LJ62	Lung, Panereas. Breast/Ovarian
670188	G protein gamma-10 subunit [Homo supiens] >pir]139158[139158 GTP-binding regulatory protein gamma-10 chain - human >splp5015 IGBGA_HUMAN GUANINE NUCLEOTIDE-BINDING PROTEIN G(I)/G(S)/G(O) GAMMA-10 SUBUNIT. Length = 68	91995919	61	238	001	100	IIWADR30	Lung. Pancreas
670279	ribosomal protein S24 [Homo sapiens] >gi 517222 ribosomal protein S24 [Homo sapiens] >gi 49652 ribosomal protein S19 (AA 1 - 133) [Mesocricctus auratus] >gi 57858 ribosomal protein S24 [Rattus norvegicus] >gi 57722 ribosomal protein S24 (AA 1-133) [Rattus	Bil337506	96	503	87		HSAYG46	Lung, Panereas. Breast/Overian
670729	acidic ribosomal phosphoprotein (P1) [Homo sapiens] >pirjB27125]R6HUP1 acidic ribosomal protein P1 - human Length = 114	gil 190234	74	496	001	100	H2CBM17	Lung. Panereas. Colon, Breast/Ovarian
674123 676496	collagen type VI, alpha 3 chain [Homo sapiens] >sp[E1292418E1292418 COLLAGEN TYPE VI, ALPHA 3 CHAIN. Length = 3176	gnlPIDje1292418	40	438	86	86	HYACISS HSLIC82	Lung, Panereas Lung, Panereas
678162	TAXREB107 [Homo sapiens] >pir 151803 151803 FAXREB107 - human Length = 288	gnilP1Did1005017	528	974	001	001	HBJJA02	Lung, Pancreas. Breast/Ovarian

HMTAK71 Lung. Pancreas	Lung, Panereas. Breast/Ovarian	Lung. Panereas. Breast/Ovarian	Lung. Breast/Ovarian	Panereas. Breast/Ovarian	Lung. Breust/Ovurian
HMTAK71	HWHGV07	HNHIWOS	HOGAV47	HISBX26	HNDAASI
001	94	000		16	001
001	94			74	001
077	1912	214	3219	089	1121
m	\$66	73	2824	471	m
gnl PID d1026577	gi 180392	gi 184407		gi 1049295	gij34388
dolichol-phosphate-mannose synthase [Homo sapiens] >sp[060762]060762 DOLICHOL-PHOSPHATE-MANNOSE SYNTHASE. >spn[PtD]d1026578 dolichol-phosphate-mannose synthase [Homo sapiens] [SUB 1-120] Length = 260	alpha 1 (1) chain propeptide [Homo sapiens] >gil180380 alpha-1 type 1 collagen [Homo sapiens] {SUB 64-201} Length = 1040	Q12 7F5 [Homo sapiens] >gi]189266 may code for Wilm's tumor-related protein [Homo sapiens] >gi]1908 H Wilm's tumor-related protein [Homo sapiens] >gi]1203971 QM gene product [Homo sapiens] >bbs]135740 QM [human, nontumorigenic Wilms' microcell hybrid c		Description: KRAB zinc finger protein; this is a splicing variant that contains a stop codon and frame shift between the KRAB box and the zinc finger region; Method: conceptual translation supplied by author [Homo sapiens] >sp[Q13359[Q13359 KRAB ZINC FING	lipocortin (AA 1-346) [Homo sapiens] >pirjA03080 LUHU annexin I - human >sp P04083 ANXI_HUMAN ANNEXIN I (LIPOCORTIN I) (CALPACTIN II) (CHROMOBINDIN 9) (P35) (PHOSPIROLIPAS): A2 INHIBITORY PROTEIN). {SUB 2-346} Length = 346
678248	683668	693172	694303	695042	699799
4	42	64	44	2	94

dihydrodiol dehydrogenase [Homo sapiens] gil452484 41 1048 95 95 >gll487135 hepatic dihydrodiol dehydrogenase [Homo sapiens] >gil 81549 dihydrodiol dehydrogenase [Homo sapiens] >gil 81549 dihydrodiol dehydrogenase (EC 1.1) - human >splQ04828 DB	HNALC11 Lung, Pancreas
pir \dss494 \dss494 3 \$87 Iomo gi 189676 29 622	
gi 452484 41 pir A55494 A55494 3	
omo	
lomo ngth	gi 452484
	dihydrodiol dehydrogenase [Homo sapiens] >gil487135 hepatic dihydrodiol dehydrogenase [Homo sapiens] >gil181949 dihydrodiol dehydrogenase [Homo sapiens] >pir1A53436 A53436 3-alpha- hydroxysteroid/dihydrodiol dehydrogenase (EC
	74

HKABK62 Lung, Pincreas	4 Lung, Panerens, Breast/Ovarian	2 Lung, Panereas, Breast/Ovarian		5 Lung. Panereus i2 Lung. Colon		Breast/Ovarian
НКАВК	HSKEP04	HPJBV92	НКАВН59	HELGY IS HCFMH52	HLJDO53	
86	09			66		1
86	45		<u> </u>	96		;
869	729	654	526	1010	661	
m .	34	-	71	228	4	•
gni P1D d1000439	gn PID c1346018		gniPIDje220196	gi 291868 gn P1D d1024640		
lipocorin II [Homo sapiens] >pir[A23942 LUHU36 annexin II - human >sp P07355 ANX2_HUMAN ANNEXIN II (LIPOCORTIN II) (CALPACTIN I HEAVY CHAIN) (CHROMOBINDIN 8) (P36) (PROTEIN IV) (PAP-IV) (SUB 2-339) >sp G545587 G545587	homology with 16.7 KD putative viral protein YUBI_NPVAC [Caenorhabdiiis elegans] Length = 250		epsilon isoform of 61kDa regulatory subunit of PP2A [Homo sapiens] >gil478070 protein phosphatase B56-epsilon [Homo sapiens] >sp[Q16537]Q16537 EPSILON ISOFORM OF 61KDA REGULATORY SUBUNIT OF PP2A. >gil1022892 protein phosphatase PP2A0 B' subunit delta is	ATPase [Homo sapiens] Length = 617 (AB009282) cytochrome b5 [Homo sapiens] >spiO43169[043169 CYTOCHROME B5	(FRAGMENT). Length = 146	
719790	720222	724033	724767	727065 727246	727932	;
\$5	96	23	88	99	19	!

		-							
63	732514	lysophosphatidic acid acyltransferase-alpha [Homo sapiens] >gi[2253613 putative lysophospholipid acyltransferase [Homo sapiens] >gnl[PID]e286645 I-acyltrjecrol-3-phosphate O-acyltransferase [Homo sapiens] >spl[099943]PLCA_HUMAN 1-ACYL-SN-GLYCEROL-3-PHOSPHA	gi2155238	m	794	56	66	HLDBX26	Prostate Prostate
64	734080			-	567			HF1BK44	Lung. Brenst/Ovarian
65	734288	cysteinyl-tRNA synthetase [Homo sapiens] Length = 595	gi 927229	154	2067	66	66	HKABU01	Lung, Pancreas
99	739448	Nascent polypeptide associated complex alpha subunit [Homo sapiens] >gil4092060 (AF054187) alpha NAC [Homo sapiens] >pir S49326 S49326 Nascent polypeptide associated complex alpha chain - human >splQ13765 Q13765 NASCENT POLYPEPTIDE ASSOCIATED COMPLEX ALPH	gi 556642	4 1	1184	. 82	82	HKGAT31	Lung. Breast/Ovarian
29	739668			2	484			HAPFL07	Lung, Pancreas
89	740060	Diff33 gene product [Homo sapicns] >splQ13530 Q13530 PLACENTAL PROTEIN DIFF33. Length = 494	gi 1293563	97	1536	94	94	HMEGB82	Lung, Panereas
69	741560			3	296			HCGM112	Lung. Colon
	742543	human gamma-glutamyl hydrolase [Homo sapiens] >splQ92820IQ92820 HUMAN GAMMA-GLUTAMYL HYDROLASE (EC 3.4.22.12). Length = 318	gi 2951931	187	804	66	001	HE2BG62	Lung, Colon. Breast/Ovarian
11	742831			25	297			IICDAL47	Panereas, Colon

745327	channel-like integral membrane protein [Homo sapiens] >gil1314304 channel-like integral membrane protein [Homo sapiens] >pirl41616[Homo sapiens] >pirl41616[Homo sapiens] >pirl41616[Homo sapiens] >splP29972]AQP1_HUMAN AQUAPURIN-CIIIP (WATER CHANNEL PROTEIN FOR RE	gi 180501	988	534	86 86	86 86	HWHPM73	Lung. Pancreas
_	90K gene product [Homo sapiens] >pir A47161 A47161 Mac-2-binding glycoprotein precursor - human >sp Q08380 Q08380 MAC-2 BINDING PROTEIN PRECURSOR. Length = 585 (AF029890) hepatitis B virus X interacting protein [Homo sapiens] >sp Q43504 Q43504 HEPATITIS	Bil2745883	66	398	100	001	IIKMLD65	Lang, Panereas. Breast/Ovarian
	B VIROS X INTERACTING PROTEIN. Length = 91		172	906			HUKF158	Lung, Panereus, Colon, Breast/Ovarian
			58	180			1113711866	Lung. Breast/Ovarian
			_	480			HEBAE80	Lung. Breast/Ovarian
			_	170			HI.1AL67	Pancreas, Prostate
	UGTrell [Homo sapiens] >pirJtCs024JtCs024 UDP-galactose transporter related isozyme 1 - human >splP78383JP78383 UGTREL1. Length = 322	8i 1669560	53	1168	87	87	HDPKG74	Lung. Panerens
	The hal 237 gene product is related to S.pombe rad21 gene product. [Homo sapiens] Length = 631	gnip1D d1008135	242	1330	94	94	HWBGB01	Lung. Puncreas

Lung, Pancreas. Colon. Breast/Ovarian	Lung, Pancreas Lung, Colon	Lung, Pancreas, Breast/Ovarian	Lung. Breust/Ovarian	Lung. Breast/Overrien	Pancreas. Breast/Ovarian
HE8AF67	IISYBW76 HCABA08	HMEJS13	НСНОІ.74	HNTAP78	НСНММ71
46	001	100	.	88	12
9 6	66	001		9	52
80 80 80	1729	166	886	1833	484
· - .	1457		7	526	7
gi 56733	gi 182658	gi 1688074	gil2702370	gi 510717	gi 3242705
myosin I heavy chain [Rattus norvegicus] >pirjA45439JA45439 myosin I heavy chain + rat >splQ05096[Q05096 MYOSIN HEAVY CHAIN I. Length = 1136	5-lipoxygenase activating protein [Homo sapiens] >pir[A39824 A39824 5-lipoxygenase-activating protein - human >spl?20292 FI.AP_IRWAN 5-	LIPOXYUENASE ACTIVATING PROTEIN (FLAP) (MK-886-BINDING PROTEIN). Length = 161 tetratricopeptide repeat protein [Homo sapiens] >spi(99614 Q99614 TETRATRICOPEPTIDE REPEAT PROTEIN. Length = 292	(AF038604) contains similarity to Drosophila ovarian tumor locus protein (GB:X13693) [Caenorhabditis elegans] >spl044438 O44438 B0546.2 PROTEIN. Length = 346	nucleur pore complex protein NUP107 [Rattus norvegicus] >pir A54142 A54142 nucleoporin NUP107 - rat >sp P52590 N107_RAT NUCLEAR PORE COMPLEX PROTEIN NUP107 (NUCLEOPORIN NUP107) (107 KD NUCLEOPORIN) (P105). Length = 926	(AC003040) putative nicotinate phosphoribosyltransferase [Arabidopsis thaliana] >spl080459 080459 PUTATIVE NICOTINATE PHOSPHORIBOSYLTRANSFERASE. Length = 574
756557	756712 757414	757614	757815	759878	760227
≅	83 83	25	82	98	84

IIMVDD07 Lung. Pancreus	Lung. Breast/Ovarian	Panereas, Colon	Pancreas. Breast/Ovarian	Lung, Panereas	Lung, Panereas, Colon, Breast/Ovarian	Lung. Pancreas	Lung. Breast/Ovarian
IIMVDD07	HMAFA79	HCECT76	171191171	НАЈАQ70	HRADN48	HAIDT44	HCEOT95
66			66	001	001	11	54
66			66	001	001	28	35
3215	627	497	625	646	1409	1562	1158
.66	-	327	251	32	1005	711	145
. \$1808\$15			gi 3170176	gni[PtD]d 1004511	gi 338228	gi 1245686	gniPiDid1018240
chondroitin sulfate proteoglycan versican V0 splicevariant precursor peptide [Homo sapiens] >splP13611PGCV_HUMAN VERSICAN CORE PROTEIN PRECURSOR (LARGE FIBROBLAST PROTEOGLYCAN) (CHONDROITIN SULFATE PROTEOGLYCAN CORE PROTEIN 2) (GLIAL HYALURONATE- BINDIN			(AF039688) antigen NY-CO-3 [Homo sapiens] >sp O60525 O60525 ANTIGEN NY-CO-3 (FRAGMENT). Length = 192	ATP synthase gamma-subunit [Homo sapiens] >gul[PID[d1004512 ATP synthase gamma-subunit [Homo sapiens] >pir[A49108]A49108 H+- transporting ATP synthase (EC 3.6.1.34) gamma chain - human >sp[P36542]ATPG_HUMAN ATP SYNTHASE GAMMA CHAIN, MITOCHONDRIAL PRECURSOR	src-like tyrosine kinase (put.); putative [Homo sapiens] Length = 537	F36D4.2 gene product [Caenorhabditis elegans] >sp[Q20100]Q20100 COSMID F36D4. Length = 224	cell division inhibitor [Synechocystis sp.] >pir S77404 S77404 cell division inhibitor - Synechocystis sp. (PCC 6803) >sp P73467 P73467 CELL DIVISION INHIBITOR. Length = 339
760312	766051	767593	768053	768055	769685	771920	772790
&	68	06	16	33	93	94	95

772916	similarto human ZFY protein. [Homo sapiens] >splQ92610 Q92610 MYELOBLAST KIAA0211. Length = 1267	gnip1Did1013891	æ	\$96	66	66	HCE1126	Lung, Panereas
773225	Urs [Homo sapiens] >gi[2731383 HGF receptor substrate Hrs [Homo sapiens] >sp O14964 O14964 HRS, COMPLETE CDS. Length = 777	gni ²ID d1024245	52 –	309	86	%	HCEVQ60	Lung, Panereas Panereas, Prostate, Breast/Ovarian
774364	(AF080561) SYT interacting protein SIP [Humo sapiens] >sp 075932 075932 SYT INTERACTING PROTEIN SIP. Length = 669	gil3746787	-	408	100	100	HCHAR77	Pancreas. Breast/Ovarian
775355	rfp transforming protein [Homo sapiens] >pir[A28101[TVHURF ret finger protein - human >gnl[PID]e308255 RFP [Homo sapicns] {SUB 250- 513} Lenglh = 513	gi 337372	1399	1781	92	92	HDTBY31 HISCU10	Lung, Panereas Lung, Panereas
092777	(AF015040) NUMB protein [Homo sapiens] > sp[G4102705 G4102705 NUMB PROTEIN. > gj4050088 (AF109907) S171 [Homo sapiens] {SUIB 79-603 > gj887362 (ORI: putative [Homo sapiens] {SUB 469-603 Length = 603	gi 4102705	62	1372	%	20	HMSIIK67	Panereas. Breast/Ovarian
779837	tazarotene-induced gene 2 [Homo sapiens] >spiQ99969[Q9969 TAZAROTENE-INDUCED GENE 2. Length = 163	gi 1848264	∞		76	86	HSWBV38	Lung, Pancreas
780769	(AF084259) bromodomain-containing protein BP75 [Mus musculus] >sp 088665 088665 BROMODOMAIN-CONTAINING PROTEIN BP75. Length = 651	gij3493162	100	762	35	58	HULBS08	Lung, Pancreus
781445			496	1443			HMVAP52	Panereas. Breast/Ovarian

Pancreus. Breast/Overien	Panereas. Breast/Ovarian	Lung. Colon	Lung, Pancreas, Breast/Ovarian	Lung, Panereas. Breast/Ovarian	Lung, Pamereas, Breast/Ovarian	Lung, Colon, Breast/Ovarian	Lung, Pancreas	Lung, Pancreas, Breast/Ovarian	Lung, Panereas	Lung. Breast/Ovarian	Lung, Pancreas. Breast/Ovarian
HCHAF71	HTPCZ45	HMWGR19	HNTNB85	HNTNQ08	IIPMC114	HCGBE06	HUSX165	HBJJB89	HUKBB89	HKAJZ91	HATBM56
001	92	88	∞	82	87					94	
00	8	85	≅	τ.	87			·		8	
486	674	616	943	696	9091	1350	509	180	975	856	402
_	. 120	413	08	-	308	67	3	64	319	80	178
gi 699577	gil1208732	gi 1763615	gnl PID e1289747	gi 177577	gi 1229140					gnl PID d1007816	
lumican [Homo sapiens] Length = 338	ovary2 [Drosophila melanogaster] >splQ27924 Q27924 OVARY2. >gi 1208729 ovary2 Drosophila melanogaster {SUB 386-545} Length = 545	myogenic repressor I-mf (Homo sapiens) >splQ99750 Q99750 MYOGENIC REPRESSOR I- MF. Length = 246	(AJ005893) JM26 [Homo sapiens] >splO60828[O60828 JM26 PROTEIN, COMPLETE CDS (CLONE LLOXNC01U138D3 (BAYLOR COLLEGE)). Length = 265	WW-domain binding protein I [Mus musculus] >sp P97764 P97764 WW-DOMAIN BINDING PROTEIN I. Length = 305	translation initiation factor 5 [Homo sapiens] >splP55010 IF5_HUMAN EUKARYOTIC TRANSLATION INITIATION FACTOR 5 (EIF-5). Length = 431					proteasome subunit z [Homo sapiens] >splQ99436 Q99436 PROTEASOME SUBUNIT 2. Length = 277	
781531	783018	783097	784198	784868	785428	785845	785854	786705	787186	787279	789002
901	107	108	. 100	011	Ξ	112	113	14	115	91	1117

8	789008	1.8 kb mRNA (AA 1-84) [Homo sapiens] >pirlS03384 S03384 hypothetical protein (IGF-II 3' region) - human >sp P09565 IGZR_HUMAN PUTATIVE INSULIN-LIKE GROWTH FACTOR II ASSOCIATED PROTEIN. Length = 84	gi 33000	1354	1737	001	001	HISCN20	Lung. Panereas
611	789555	(AL035247) hypothetical trp-asp repeat protein [Schizosaccharomyces pombe] Length = 760	gni PID e1371207	124	1815	42	99	HTTCB23	Pancreas, Breast/Ovarian
120	789631			192	320			III.ICN93	Lung, Panereus,
121	789779			-	396			HCHMS40	Colon. Genst/Overtien
122	790387			٣	527			HLMINA32	Colun. Breast/Ovarian
123	790461	(AF008445) phospholipid scramblase [Homo sapiens] >gnlPID[d1033532 (AB006746) hMmTRA ib [Homo sapiens] >gild092081 (AF098642) phospholipid scramblase; plasma membrane phospholipid scramblase [Homo sapiens] >splO15162 O15162 PHOSPHOLIPID SCRAMBLASE. >splG4	gi 2282601	105	1193	66	66	HTGAVIO	Lung. Panereas. Breust/Ovarian
124	790931			7	394			HBCA030	Pancreas.
125	791176	(AB002107) hPer [Homo sapiens] >gi 2435507 (AF022991) Rigui [Homo sapiens] >sp O15534 O15534 RIGUI. Length = 1290	dbj AB002107_1	m	1034	06	06	IINFCJ67	dreas/Ovarian Lung, Panereas
126	791983			637	837			HBJLE45	Lung, Pancreas, Colon, Breast/Ovarian

					•
Lung, Puncreas, Breast/Ovarian	Lung. Brass/Ovarian	Lung. Breust/Ovarian	Lung, Panereas	Lung, Pancreus. Breust/Ovarian	Lung. Panereas
НБРРХ89	HDQEP64	HMEKG25	ITWFN71	HJAAE81	HWABS13
94	. 96	98	66	001	66
94	95	\$	66	<u>0</u>	66
1068	1104	1305	1365	101	. 640
P6	34	778	889	E .	119
gil2460200	gi 1390025	gi 2674195	. gnilP1D c1311294	gi 287641	gni[PID d1010153
(AF020833) eukaryotic translation initiation factor 3 subunit [Homo sapiens] >sp[O14801[O14801] EUKARYOTIC TRANSLATION INITIATION FACTOR 3 SUBUNIT. Length = 320	protein arginine N-methyltransferase [Rattus norvegicus] >splQ63009 ANM RAT PROTEIN ARGININE N-METHYLTRANSFERASE (EC 2.1.1). Length = 353	(AF036249) polymerase I-transcript release factor, PTRF [Mus musculus] >sp\054724\054724 POLYMERASE I AND TRANSCRIPT RELEASE FACTOR (POLYMERASE I-TRANSCRIPT RELEASE FACTOR). Length = 392.	dJ1409.2 (Melanoma-Associated Antigen MAGE LIKE) [Homo sapiens] >sp 076058 076058 DJ1409.2 (MELANOMA-ASSOCIATED ANTIGEN MAGE LIKE). Length = 606	proliferation associated gene (pag) gene product [Homo sapiens] >pir[A46711]A46711 proliferation associated gene (pag) protein - human Length = 199	alpha mannosidase II isozyme [Homo sapiens] >splP49641 MA2X_HUMAN ALPHA-MANNOSIDASE IIX (EC 3.2.1.114) (MANNOSYL-OLIGOSACCHARIDE 1,3-1.6-ALPHA-MANNOSIDASE) (MAN IIX). Length = 1139
792539	792749	792961	793206	793249	793626

creas. arian	ırian	ırian	reas	nrian	reus, olon, irian	reus. irian	irian	ırian
Lung, Panereas. Breast/Ovarian	Lung. Breast/Ovarian	Pancreas, Breast/Ovarian	Lung. Panereas	Colon. Breast/Ovarian	Lung, Panereas, Prostate, Colon, Breast/Ovarian	Lung, Pancreus, Breast/Ovarian	Colon. Breast/Ovarian	Pancreas. Breast/Ovarian
ПРВКОЗ	HDPP:726	HE8F192	HWBDR92	нснРФ06	HPMSD56	HEONK47	11C11AM08	HEMFP05
66		16		87	94			200
· 66		16		8.4	94			83
1142	888	1531	1018	851	1107	1553	126	098
. "	82	101	2	٣	49	525	-	282
gi[2906146		gi 1051170		pir B42856 B42856	gil699577			gi 1518918
(AF047470) malate dehydrogenase precursor [Homo sapiens] >sp[O43682]O43682 MALATE DEHYDROGENASE (EC. 1.1.1.37) PRECURSOR (EC. 1.1.1.37). Length = 338		GAP SH3 binding protein [Homo sapicns] >splQ13283 Q13283 GAP SH3 BINDING PROTEIN. Length = 466		ubiquitin carrier protein E2 - human >gi 181916 ubiquitin carrier protein [Homo sapiens] {SUB 23- 247} Length = 247	lumican [Homo sapiens] Length = 338			DNAJ homolog [Homo sapiens] >gi 1127833 heat shock protein hsp40 homolog [Homo sapiens] >pir G02272/G02272 heat shock protein hsp40 homolog - human >sp Q13431 Q13431 HEAT SHOCK PROTEIN HSP40 HOMOLOG. Length = 178
794417	795197	795251	795752	796261	796933	799424	799698	800351

l.ung. Breast/Ovarian	Lung. Colon.	Lung, Pancreas	Lung, Panereas	Line Pancress	Lung, Pancreas, Colon, Breust/Ovarian	Lang. Breast(Ovarian	Colon. Breast/Ovarian
HCEVS28	HC11AP80	HTELC67	HNTDX22	HISEALI	HLWAW17	ווטקויאבאיוטקוו	нгуек93
8			75				16
93			19			06	98
. 1383	1055	1028	741	88	234	887	1511
178	15	711	226	891	13	m	1338
gniPIDjc235521			gi 4050034			gni P1D d1007285	gi 1353711
26S protease subunit [Sus scrofa] >gi]3193258 (AF069053) proteasome subunit SUG1 [Bos taurus] >gn PtD d1012606 proteasomal ATPase (rat SUG1) [Rattus norvegicus] >gn PtD d1023806 (AB000491) proteasome p45/SUG [Rattus norvegicus] >gn PtD c199326 mSUG1 pr			(AF098482) transcriptional coactivator p52 [Homo sapiens] >sp[G4050034 G4050034 TRANSCRIPTIONAL COACTIVATOR P52. Length = 333			cytokine inducible SH2-containing protein [Musmusculus] >pit/S5551[S5551 cytokine-inducible protein CIS - mouse >spiQ62225[Q62225 CYTOKINE INDUCIBLE SH2-CONTAINING PROTEIN (SH2 DOMAIN CONTAINING PROTEIN INDUCED BY MULTIPLE CYTOKINES, SIC). Length = 257	FIN14 gene product [Mus musculus] >sp Q61077 FI14_MOUSE FIBROBLAST GROWTH FACTOR INDUCIBLE PROTEIN 14 (FIN14). Length = 61
800573	805815	806445	810309	811022	811023	811143	811381
142	143	144	145	146	147	2	149

Pancreas. Breast/Ovarian	Pancreas.	Lung. Breast/Ovarian	Lang, Pancreas	Lung. Panereas	Lung, Pancreas. Breast/Ovarian	Lung, Pancreas
HDTLA92	HDPVZ64	нспмџез	нжно.	нсевл3	HAJBH20	HDABR53
001	98 .	· 98	88	001	001	100
100	%	98	68	001	86	. <u>00</u>
609	850	510	470	651	1398	496
_	95	-	m	_		7
gniPID d1011874	gi 1575505	gij31303	gi 434845	Bi 55651	gi 1016275	gi404015
CIRP [Homo sapiens] >gij2924760 (AC004258) CIRP [Homo sapiens] >gij2541973 (AF021336) DNA damage-inducible RNA binding protein [Homo sapiens] >sp[Q14011Q14011 GLYCINE- RICH RNA BINDING PROTEIN CIRP. Length = 172	Tera [Mus musculus] >splP70361[P70361 TERA. Length = 277	fau gene product [Homo sapiens] >gi[31305 fau I gene product [Homo sapiens] >pir[JC1278]JC1278 ubiquitin-like protein / ribosomal protein S30, cytosolie - human Length = 133	DAP-1 [Homo sapiens] >pirl137274 137274 death-associated protein 1 - human >splP\$1397 DAP1_HUMAN DEATH-ASSOCIATED PROTEIN 1 (DAP-1). Length = 102	PISSLRE gene product [Homo sapiens] >pir[S49330]S49330] serine/threonine kinase (EC 2.7.1) pissire - human >pir]138116[138116 gene PISSLRE protein - human >sp[Q15131]Q15131 PISSLRE MRNA. Length = 360	retinoblastoma-binding protein mRbAp48 [Mus musculus] >pir 149366 149366 retinoblastoma-binding protein mRbAp48 - mouse Length = 46	ribosomal protein L23a [Homo sapiens] >gi 306549 homology to rat ribosomal protein L23 [Homo sapiens] {SUB 10-156} Lcngth = 156
811595	813000	813288	813431	813450	813478	813505
130	151	152	153	154	155	156

157	815552	(AJ011497) Claudin-9 [Homo sapiens] >>p E1363658 E1363658 CLAUDIN-9. Length = 211	gni PID e1363658	317	868	95	96	HUFEH29	Lung. Colon	
158	815606	Ki-1/57 intracellular antigen [Homo sapiens] >spi075804(075804 Ki-1/57 INTRACELLULAR ANTIGEN (FRAGMENT). Length = 299	gi 3403154	218	1303	06	. 95	HDPRY63	Lung, Pancreas, Breast/Ovarian	
159	816048	neutral protease alpha subunit [Homo sapiens] >gi]35328 protease small subunit (aa 1-268) [Homo sapiens] >gi]1905903 (AD001527) calciumdependent protease, small (regulatory) subunit (calpain) (calcium-activated neutral proteinase) (CANP) [Homo sapiens] >	9006 Llis	24	644	95	96	HTLCZ60	Lung. Breast/Ovarian	
160 161 162	822978 823616 823981	(AF003130) similar to Achlya ambisexualis antheridiol steroid receptor (NID:g166306) (Caenorhabditis elegans) >sp[001757]001757	gi 2088668	94 1449 992	156 1775 2617	. 09	78	HODEM46 HCEME79 HWHQH79	Lung, Panereas Panereas, Colon Lung, Breast/Ovarian	
	824364	SIMILAR 10 ACHLYA AMBISEXUALIS ANTHERIDIOL STEROID RECEPTOR. Length = 1043 drebrin E2 [Homo sapiens] >gnl PID d1005005 drebrin E (Homo sapiens] >pirJN0809JN0809 drebrin E (clone gDbh13) - human >splQ16643JDREB_HUMAN DREBRIN E. Length = 649	gi 392890	- .	. 909	2 8	3	нснекза	Colon. Breast/Ovarian	

,					
Lung. Panereas	Lung, Panereus Colon, Breast/Ovarian	Lung. Breast/Ovarian	Lung, Pancreas	Lung. Colon Breust/Ovarian	Lung. Breast/Ovarian
HPWDI.83	HEDN61 HTODA45	HI.UDB77	HMWIV57	HPTVX93	HDAAD02
99		₹		100	88
<u>e</u>		=	66	001	1
1743	602	1504	723	961	2176
19	36	473	25	∹	53
gi 971459		gi 517822	gniPIDle1188703	gi 1071681	gn PID e1198294
UDP-GalNAc:polypeptide N-ucctylgalactosaminyl transferase [Homo sapiens] >pirJC4223JJC4223 polypeptide N-ucctylgalactosaminyltransferase (EC 2.4.1.41) - human >spQ1040472JPAGT_HUMAN POLYPEPTIDE N-ACETYLGALACTOSAMINYL:TRANSFERASE (EC 2.4.1.41) (PROTEIN- UDP		ancient ubiquitous 46 kDa protein AUP46 precursor [Mus musculus] >sp[P70295[P70295 ANCIENT UBIQUITOUS PROTEIN PRECURSOR (AUP1). Length = 410	hNop56 [Homo sapiens] >sp[000567]NO56_HUMAN NUCLEOLAR PROTISIN NOP56. Length = 602	H. sapiens mRNA for rat translocon-associated protein delta homolog [Homo sapiens] >gnl[PIDje212192 translocon-associated protein delta subunit precursor [Homo sapiens] >gnl[PIDje220312 translocon-associated protein delta subunit precursor [Homo sapiens]	(AL009171) 62D9.a [Drosophila melanogaster] >sp[E1198294[E1198294] = 1305
824423	825279 825442	825548	825725	826639	827079
164	165	167	891	691	170

Pancreas, Colon, Breast/Ovarian	Colon.	Lung. Breast/Ovarian	Colon. Breast/Ovarian	Lung. Panereas. Colon. Breast/Ovarian	Lung, Pancreas	Lung, Punerens,	Prostate, Colon
HI.QBS95	HSKJE35	HLAAB36	HBGDHII	HCHAK72	HMSOT38	HTECA53	HWI.A1178
8		8	16	89	27		
06		%	. 28	55	62		
602	639	1886	776	744	836	1305	1314
. 42	_	255	9	-	165	1147	1105
gi 482909		gi 3264574	gi 1176422	gi 2507613	gi 289610		
pancreatitis-associated protein [Homo sapiens] >gij312807 preprotein [Homo sapiens] >bbs 121222 PAP-H=pancreatitis-associated protein [human pancreas, Peptide, 175 aa] [Homo sapiens] >gin PID d1003233 PAP homologous protein [Homo sapiens] >pir A49616 A49		(AC004003) serine/threonine kinase RICK; match to protein AF027706 (PID:g3123887) and mRNA AF027706 (NID:g3123886) [Homo supiens] >gi]3290172 (AF064824) CARD-containing ICE associated kinase [Homo supiens] >gi]3342910 (AF078530) receptor interacting prote	rhophilin [Mus musculus] >splQ61085 Q61085 GTP-RHO BINDING PROTEIN 1 (RHOPHILIN). Length = 643	serine protease [Homo sapiens] Length = 492	homology with GTP binding protein; putative [Caenorhabditis elegans] >pir[S44605 S44605 C02F5.3 protein - Caenorhabditis elegans Length = 573		
827153	827351	827503	827563	827565	827893	828072	828228
171	27.1	173	174	175	176	177	178

179	828241	cathepsin O [Homo sapiens] >pir[A55090]A55090 cathepsin O (EC 3.4) precursor - human >splP43234 CATO_HUMAN CATHEPSIN O PRECURSOR (EC 3.4.22) Length = 321	gi 574804	6	1012	93	93	HWBBP30	Lung, Panereas. Prostate
081	828287	histone (H2A.Z) [Bos taurus] >gil410 histone H2A.Z (AA 1-127) [Bos taurus] >gil484060 histone (H2A.Z) [Homo sapiens] >gil31975 histone H2A.Z (AA 1-127) [Homo sapiens] >gil3649600 histone [Homo sapiens] >gil204599 histone (H2A.Z) [Rattus norvegicus] >gil57	gi 163150	171	572	001	901	HUSIS02	Lung, Panereas. Prostate: Breast/Ovarian
<u>8</u>	828364			663	1340			HWHGT17	Pancreus. Report/Overing
	828371	complement component C1s [Homo sapiens] >gi179648 complement subcomponent C1s precursor [Homo sapiens] >gi763110 complement protein C1s precursor [Homo sapiens] >pir/A40496[C1HUS complement subcomponent C1s (EC 3.4.21.42) precursor - human >spiP09871[C1	gi 179646	च	2283	76		HLQCQ12	Lung. Panerens. Colon. Breast/Ovarian
83	828403	DNA-binding protein [Homo sapiens] >pir A44478 A44478 probable cell growth or differentiation regulator (alternatively spliced type I transcript) - human >sp Q02833 Q02833 PUTATIVE TRANSCRIPTIONAL REGULATORY PROTEIN HRC1. Length = 373	gi 184390	- .	648	86	86	нртиц82	Lung, Panereas. Colon
184	828501	(AF056302) eIF-2alpha kinase [Drosophila melanogaster] >sp 061651 061651 EIF-2ALPHA KINASE, Length = 1589	gi 3046551	_	1812	36	28	HBMDG73	Lung, Colon, Breast/Ovarian

Prostate, Breast/Ovarian	Lung, Panereas. Prostate. Breast/Ovarian	Lung, Prostate, Breast/Ovarian	Panerens. Prostate, Colon	Panereas, Colon	Pancreas. Prostate	Pancreas. Prostate, Colon	Lung, Prostate	Pancreus, Prostate. Colon
HRGBN47	HSKGQ05	HPWDF55	HRACJ32	HFIAL22	HPWBR24	HPTVU91	HPRAT58	HPRCM33
1 6			001	P6				94
16			001	94				76
1821	926	926	933	1738	342	131	1568	1029
445	723	332		26	<u>-</u> ·	e.	1050	307
gnilPID c1321519			gi 35799	gi]307506				gi 180926
(AJ010840) A'TP-dependent RNA helicase [Homo sapiens] >sp[E1321519 E1321519 ATP-DEPENDENT RNA HELICASE (FRAGMENT). Length = 420			pre-pump-1 proteinase (AA -17 to 250) [Homo sapiens] >gi[35803 PUMP [Homo sapiens] >pir[B28816 KCHUM matrilysin (EC 3.4.24.23) precursor - human >sp P09237 COG7_HUMAN MATRILYSIN PRECURSOR (EC 3.4.24.23) (PUMP-1 PROTEASE) (UTERINE METALLOPROTEINASE) (MATRI	thrombospondin 2 [Homo sapiens] >pir[A47379[TSHUP2 thrombospondin 2 precursor - human Length = 1172				tumor-associated antigen [Homo sapiens] >pirlA36056[A36056 tumor-associated antigen CO- 029 - human >sp[P19075]CO02_HUMAN TUMOR-ASSOCIATED ANTIGEN CO-029.
828520	828527.	828538	828541	828549	828562	828576	828602	828628
<u>25</u>	981	187	<u>8</u>	681	061	<u> </u>	192	193

Panereas. Breast/Ovarian	Pancreas, Prostate	Lung, Prostate. Breast/Ovarian	Pancreas. Colon. Breast/Ovarian	Pancreas. Prostate, Breast/Ovarian
HKAOB02	IIPJAE35	нмсвв12	HSRAB84	HPIACII
2 2	92	93	66	000
%	92	93	8	001
9001	1573	629	657	546
5	4	m		n
gi 181240	gi 468032	gi 4164442	gil1107687	gil2909830
cytochrome c-1 [Homo sapiens] >sp P08574 CY1_HUMAN CYTOCHROME C1, HEME PROTEIN PRECURSOR. >gi1181238 cytochrome c1 [Homo sapiens] {SUB 99-325} Length = 325	p55CDC [Homo sapiens] >pirlA56021 A56021 probable cell division control protein p55CDC - human >sp Q12834 Q12834 P55CDC. Length = 499	(AF044954) NADH:ubiquinone oxidoreductase PDSW subunit [Homo sapiens] >gil4165091 (AF088991) NADH-ubiquinone oxidoreductase PDSW subunit [Homo sapiens] Length = 172	homologue of Drosophila Fat protein [Homo sapiens] >splQ14517[Q14517 CADHERIN-RELATED TUMOR SUPPRESSOR HOMOLOG PRECURSOR (FAT PROTEIN HOMOLOG) >gn PID d1022418 cadherin [Homo sapiens] {SUB 993-1132} 1.cngth = 4590	(AF035940) similar to mago nashi [Homo sapiens] >gi[2330011 (AF007862) mm-Mago [Mus musculus] >gi[2909828 (AF035939) similar to mago nashi [Mus musculus] >splC035169[035169] MM-MAGO. >splC2909830[G2909830 MAGOH. >splF50606[MGN_HUMAN MAGO NASHI PROTEIN HOMOL.
828667	828684	828727	828734	828750
194		961		86 1

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Pancreus, Prostate, Breast/Ovarian	Lung, Panereas. Prostate	Panereus. Prostate	Prostate. Breast(Ovarian	Prostate, Breast/Ovarian	Lung, Pancreas, Colon
HOUGAI2	HOVBK85	H0SGA73	нонеи75	HOHBI90	HOEKU65
001	001	86		86	94
86	66	86	66	86	94
363	761	1029	804	417	1279
-	m ·	-	-	-	32
gni P1D d1023271	gi 904032	gi 4033735	Bi 339709	gi(292870	gi 37265
(AB007191) AMY-1 [Homo sapiens] >gn PID d1009980 c-myc binding protein [Homo sapiens] >sp Q99417 Q99417 C-MYC BINDING PROTEIN. Length = 103	p48 [Homo sapiens] >splP50502[HIP_HUMAN HSC70-INTERACTING PROTEIN (PROGESTERONE RECEPTOR-ASSOCIATED P48 PROTEIN). >gi 1857033 SCN6 gene product [Homo sapiens] {SUB 99-369} Length = 369	(AF054284) spliceosomal protein SAP 155 [Homo sapiens] >splG4033735 G4033735 SPLICEOSOMAL PROTEIN SAP 155. >gij3387899 (AF070540) putative nuclear protein [Homo sapiens] {SUB 1011-1304} Length = 1304	thymidine kinase (EC 2.7.1.21) [Homo sapiens] >gi[339719 thymidine kinase [Homo sapiens] >pir[A27318]KIHUT thymidine kinase (EC 2.7.1.21), cytosolic - human >splP04183]KITH_HUMAN THYMIDINE KINASE, CYTOSOLIC (EC 2.7.1.21). >gi[339713 thymidine kinase [Homo	tyrosine kinase receptor [Homo sapiens] > pir[B41527]B41527 transforming protein (axl(-)) - human Length = 885	TRAM protein [Homo sapiens] >pir[S30034 S30034 translocating chain-associating membrane protein human >splQ15629 Q15629 TRAM PROTEIN. Length = 374
828842	828843	828851	828856	828862	828870
661	200	201	202	203	204

Lung, Pancreas, Prostate, Colon, Breast/Ovarian	Lung, Prostate. Breast/Ovarian	Panereus. Prostate, Colon. Breast/Ovarian	Panerwas, Colon. Breast/Ovarian
HOHCJ26	HOGAA83	HOGA S09	HBCAY53
001	. .	\$ 8	95
901	06	98	92
1398		1253	118
-	٣	36	65
gi 37465	gnl PID e321549	gi 1754538	gil 143194
precursor polypeptide (AA -31 to 1139) [Homo sapiens] >gi 538354 thrombospondin [Homo sapiens] {SUB 1-397} >gi 339669 thrombospondin [Homo sapiens] {SUB 1028-1170} >gi 532689 thrombospondin-1p180 [Homo sapiens] {SUB 364-422} Length = 1170	keratin [Homo sapiens] >splQ14533 Q14533 KERATIN (HAIR TYPE II BASIC KERATIN) (KERATIN LIKE). >gnl PID e118093 hair 1ype II basic keratin [Homo sapiens] {SUB 81-505} >gi 951272 keratin like [Homo sapiens] {SUB 249- 505} >bbs 161491 type II hair keratin {cl	ESX [Homo supiens] >gi[1841523 ESE-1h [Homo sapiens] >gi[23387.56 (AF017307) Eis-related transcription factor [Homo sapiens] >gi[2387440 AF016295) Ets transcription factor [Homo sapiens] >gi[2459797 epthelial-specific ets protein [Homo sapiens] >splP78545	prostasin [Homo sapiens] > gig62305 prostasin [Homo sapiens] > pir/A57014/A57014 prostasin (EC 3.4.21) precursor - human > splG565130 G565130 PROSTASIN=SERINE PROTEINASE {N-TERMINAL; {SUB 45-64} Length = 343
828873	828892	828893	828897
205	506	207	208

nolon	rian	reas.	rens.	rian rian
Prostate, Colon	Lung Breast/Ovarian	Lung, Panereus, Prostate, Breast/Ovarian	Lung, Panereus.	Dreasty, Varian Lung, Pancreas, Colon, Breast/Ovarian
HOIIDY41	ннгли88	HNTAC57	HEMCA07	HMGBJ25
86	66	S	86	47
96	66	83	67	59
540	567	1026	852	729
. 58	-	ç	439	-
gi 455109	gil695360	ध्रां182855	gi 531171	gil1008304
light chain 3 subunit of microtubule-ussociated proteins 1A and 1B [Rattus norvegicus] -pir[A53624 A53624 microtubule-associated protein 1 light chain 3 - rat -spiQ62625 MPL3_RAT MICROTUBULE- ASSOCIATED PROTEINS 1A/1B LIGHT CHAIN 3 (MAPIA/MAPIB LC3). {SUB	cytochrome c oxidase subunit Va [Homo sapiens] >pir[JT0342]OTHU5A cytochrome-c oxidase (EC 1.9.3.1) chain Va precursor - human >sp[P20674]COXA_HUMAN CYTOCHROME C OXIDASE POLYPEPTIDE VA PRECURSOR (EC 1.9.3.1) >gi]3859864 (AF067635) cytochrome c oxidase su	80K-II protein [Homo sapiens] >gi]1293640 protein kinase C substrate 80K-H [Homo sapiens] >pi]A32469JA32469 80K protein H precursor human >sp[P14314]G19P_HUMAN PROTEIN KINASE C SUBSTRATE, 80 KD PROTEIN. HEAVY CHAIN (PKCSH) (80K-H PROTEIN). Length = 527	Csa-19 [Homo sapiens] Length = 217	ORF YJL I 15w [Saccharomyces cerevisiae] >gi 171091 ASF1 [Saccharomyces cerevisiae] >pir S30766 S30766 ASF1 protein - yeast (Saccharomyces cerevisiae) >sp P32447 ASF1_YEAST ANTI-SILENCING PROTEIN I. Length = 279
828910	828927	828932	828933	828941
209	210	211	212	213

Prostate. Breast/Ovarian	Lung, Prostate, v Colon, Breast/Ovarian	Pancreas. Prostate, Colon. Breast/Ovarian	Lung, Panereas. Prostate. Breast/Ovarian	Panereas. Prostate. Breast/Ovarian	Lung, Panereas, Prostate, Breast/Ovarian
HMWHG54 Prostate. Breast/O	HMWBH91	HMWFZ60	HMWFV54	HMUBT12	HMVAW27
89	77		86	86	001
37	55		86	86	100
635	1293	908	1372	1535	685
æ	73	639	7	m	74
gni P1D e1346411	ا193871 نال		gil178279	gi 2102679	gi 179477
F31C3.5 [Caenorhabditis elegans] >sp 062193 062193 F31C3.5 PROTEIN. Length = 180	house-keeping protein [Mus musculus] >pir[S27870]S27870 house-keeping protein - mouse >splQ61669]Q61669 HOUSE-KEEPING PROTEIN 1. Length = 396		S-adenosylhomocysteine hydrolase [Homo sapiens] >pir A43629 A43629 adenosylhomocysteinase [EC 3.3.1.1) - human Length = 432	putative tRNA synthctase-like protein [Homo sapiens] >gil4104935 (AF042347) putative phenylalanyl-tRNA synthetase alpha-subunit: PheHA [Homo sapiens] >sp[E317305]E317305 PUTATIVE TRNA SYNTHETASE-LIKE PROTEIN >sp[G2102679]G2102679 PUTATIVE TRNA SYNTHETASE.	insulin-like growth factor binding protein 2 [Homo sapiens] >bbs]106618 insulin-like growth factor binding protein-2, IGFBP-2 [human, placenta. Peptide, 328 aa] [Homo sapiens] >pir[A41927[A41927 insulin-like growth factorbinding protein 2 precursor - hum
828957	828963	828964	828966	828967	828977

Lung, Pancreus, Prostate	Lung, Pancreas. Prostate, Colon, Breast/Ovarian	Lung, Panereas, Prostate, Breast/Ovarian	Lung. Panereis. Prostate	Prostate. Breast/Ovarian	Prostate. Colon
HNTMH78	ПМИВО53	HMSJR30	HMSKA53	IIMIAI73	HMIBES9
001			66	87	100
001			66		001
<u> </u>	1080	1959	2536	759	577
213	91	1621	635	409	7
gi 178699			gi 736249	dbj AB006625_1	188061 ig
annexin IV (placental anticoagulant protein II) [Homo sapiens] >gallPID[d1011889 annexin IV (carbohydrate-binding protein p33/41) [Homo sapiens] >pir[A42072]A42077 annexin IV - human >spiP09525[ANX4_HUMAN ANNEXIN IV (LIPOCORTIN IV) (ENDONEXIN I) (CHROMO)B			plasma gelsolin [Homo sapiens] >pir[A03011 FAHUP gelsolin precursor, plasma - human >sp P06396 GELS_HUMAN GELSOLIN PRECURSOR, PLASMA (ACTIN- DEPOLYMERIZING FACTOR) (ADF) (BREVIN) (AGEL). >gnl P1D e20565 plasma gelsolin (AA 49- 117) [Homo sapiens] (SUB 49-11	(AB006625) The human homolog of a mouse imprinted gene, Peg3. [Homo sapiens] >splP78418[P78418 KIAA0287 (PEG3) (FRAGMENT) >gi 1899244 PEG3 [Homo sapiens] {SUB 518-1132} Length = 1132	ras-like protein [Homo sapiens] >pirJD34788[TVHUC4 transforming protein ras (teratocarcinoma clone TC10) - human Length = 213
828978	828979	829001	829003	829016	829027
220	221	222	223	224	225

226	829028	RnudC gene product [Rattus norvegicus] >pir A55897 A55897 prolactin-induced T cell protein c15 - rat >sp Q63525 Q63325 C15 MRNA. Length = 332	8il619907		1110	95	86	нмсвQ56	Paneras, Prostate. Breast/Ovarian
227	829031	protocadherin X [Mus musculus] >splG4099533 G4099553 PROTOCADHERIN X. Length = 928	gi 4099553	91	637	06	93	HMGB169	Lung, Panereas. Prostate. Breast/Ovarian
228	829034			28	1362			HMEIY69	Pancreas. Prostate
229	829036	Similar to B. subtilis Poly(A) polymerase (SW:PAPS_BACSU) [Caenorhabditis elegans] >spiQ93795[Q93795 F55B12.4 PROTEIN. Length = 440	gni PID e1347205	114	151	67	-	HMEL.175	Panereas. Prostate
230	829049	UDP-Gal:GlcNAc galactosyltransferase [Homo sapiens] >splO60910jO60910 UDP-GAL:GLCNAC GALACTOSYLTRANSFERASE. Length = 393	gni PID e1283714	233	1444	94	94	НМЕ FQ33	Prostate, Colon
231	829073			193	843			HLYCD85	Pancreas, Prostate
232	829075			7	484			НМАЛД66	Lung. Pancreas. Prostate. Breast/Ovarian
233	829076			m	999			HADDC41	Lung, Pancreas. Breast/Ovarian
234	829080			m	200			IIMABG80	Prostate. Breast/Ovarian
235	829087	small GTP-binding protein [Oryctolagus cuniculus] >pir[A48500]A48500 small GTP-binding protein Rab25 - rabbit Length = 213	gi 436001	157	873	95	76	HL.WBY67	Panereas, Prostate, Breast/Ovarian

Pancreas. Prostate	Lung, Panereas. Prostate, Colon, Breast/Ovarian	Prostate. Breast/Ovarian	Lung, Prostate	Ling, Panereas, Prostate	Lung, Pancreas, Prostate, Colon	Lung, Pancreas, Breast/Ovarian	Lung. Panereus	Prostate, Breast/Ovarian
HLWBC74	III.WBM89	HLWA028	HLSDA35	HLK UR2	HLFBF56	HSPBG80	П ОВ К 92	HL1SB22
88		6	66	86	83		001	
82		76	66	. 95	83		100	
513	425	1628	415	1231	769	930	66.2	913
-	m .	552	7	215	7	403	m .	515
gn P1D d1013353		bbs 158840	gnl P1D e322419	gn PfD d1003846	gi 1064914		Bil 190500	
UDP-galactose translocator [Homo sapiens] >pir JC4903 JC4903 UDP-galactose transporter, splice form I - human Length = 393		antiquitin=26g turgor protein homolog [human, kidney, Peptide, 511 aa] [Homo sapiens] >pirA54676 A54676 antiquitin - human >splP49419 DHAX_HUMAN ANTIQUITIN (EC 1.2. 1). Length = 511	nuclear autoantigen fo 14 kDa [Homo sapiens] >spl043805[043805 NUCLEAR AUTOANTIGEN FO 14 KDA. Length = 119	unknown protein precursor [Homo sapiens] >pir[JN0596]JN0596 fibrinogen-related protein HFREP-1 precursor - human >sp[Q08830]Q08830 FIBRINOGEN-LIKE PROTEIN 1 PRECURSOR. Length = 312	ubiquitin-conjugating enzyme UbcH6 [Homo sapiens] Length = 193		C4b-binding protein alpha chain [Homo sapiens] >gil190502 C4b-binding protein alpha chain [Homo sapiens] >pirlA33568 NBHUC4 C4b-binding protein alpha chain precursor - human >sp PQ4003 C4BP_HUMAN C4B-BINDING PROTEIN ALPHĀ CHAIN PRECURSOR (PROLINE-RICH PRO	
829092	829095	829096	829118	829152	829160	829163	829176	829204
236	237	238	239	240	241	242	243	244

245	829207			Ξ	716		,	HL1SA66	Prostate.
246	829228			_	2508	•		HKGBQ77	Breast/Ovarian Lung, Prostate, Colon
247	829252			96	1322			IIKAPI21	Panereas, Prostate
248	829254			_	483			HKFB196	Lung, Pancreas. Prostate, Breast/Ovarian
249	829269			121	474			HKAEE96	Lung, Panereas, Prostate, Colon, Breast/Ovarian
250	829277			٣	596			HJPCG91	Lung, Prostate
251	829290			001	207			HJBDL52	Lung, Pancreas. Prostate, Breast/Ovarian
252	829294			m	1847			HISDU47	Panereas. Prostate
253	829299			m	794			HISEC32	Lung, Pancreus. Prostate
254	829308	dJ 1409.2 (Melanoma-Associated Antigen MAGE LIKE) [Homo sapiens] >spl076058 076058 DJ 1409.2 (MELANOMA-ASSOCIATED ANTIGEN MAGE LIKE). Length = 606	gni PID c1311294	207	938	7	70	HIBCN93	Lung, Panerens. Prostate, Colon. Breast/Ovarian
255	829349	ribosomal protein S15a [Rattus norvegicus] >pir JC2234 JC2234 ribosomal protein S15a - rat Length = 130	gi 495273	152	547	001	100	HICAF44	Lung. Panereas. Prostate. Breast/Ovarian
256	829354	RAD4 gene product [Saccharomyces cerevisiae] Length = 730	gi 4271	_	1113	44	65	HAJBDSI	Lung, Panereas, Breast/Ovarian

Lung, Pancreas, Colon, Breast/Ovarian	Lung, Pancreas, Colon, Breast/Overian	Lung, Pancreas. Colon, Breust/Ovarian	Pancreas. Breast/Ovarian	Lung, Prostate	Pancreas. Prostate	Panereas. Prostate	Lung, Puncreus. Prostate, Breast/Ovarian
HUVCJ22	HAPOU28	HCEES14	HAJBK53	HAMFJ43	HAIC'176	HAIBS55	HACCB64
94		&	\$7		98	93	
94		25	62	.	98	93	
1281	437	764	1153	1053	\$40	952	8 4
319	258	m	455	64	_	230	551
gi 929628	·	pirlB54408 B54408	gnl PID e252512	si3598795	gi 3342794	gi 3249005	
DNase protein [Homo sapiens] > gi 1620214 XIB [Homo sapiens] > pirJC4633 JC4633 DNase I-like endonuclease (EC 3.1) - human > sp P49184 DRNIHUMAN MUSCLE-SPECIFIC DNASE I-LIKE PRECURSOR (EC 3.1.21) (DNASE X) (XIB). Length = 302		mannosyl-oligosaccharide 1,2-alpha-mannosidase (EC 3.2.1.113) - rabbit (fragment) >gi 474282 mannosyl-oligosaccharide alpha-1,2-mannosidasc [Oryctolagus cuniculus] {SUB 12-480} Length = 480	underexpressed in thyroid tissue after TSH stimulation [Canis familiaris] >sp Q28283 Q28283 C5FW PROTEIN. Length = 343	(AF053651) cellular apoptosis susceptibility protein [Homo sapiens] >spl075432 075432 CELLULAR APOPTOSIS SUSCEPTIBILITY PROTEIN. Length = 971	(AF035606) calcium binding protein [Homo sapiens] >sp 075340 075340 CALCIUM BINDING PROTEIN, Length = 191	(AF067855) geminin [Homo sapicns] >splO75496 073496 GEMININ. Length = 209	
829388	829540	829626	829730	829892	829933	829938	829969
257	. 258	259	260	261	262	263	. 264

Prostate. Breast/Ovarian	Lung, Prostate, Breast/Ovarian	Prostate Breast/Ovarian	Lung, Panereas. Breast/Ovarian	Lung, Prostate, Breast/Ovarian	Lung, Panereas. Prostate, Colon,
HABGE25	H6EDW66	112МАС92	HBWBK27	H2LAD55	H2CBP53
100	66	96			
001	66	76 .			
399	9001	976	069	171	1290
	0 -	t	-	-	92
yi 2655055	gi 180920	gi(2623168			
(AF020352) NADH:ubiquinone oxidoreductase 15 kDa IP subunit [Homo sapiens] >gi[291,1482 (AF047434) NADH-ubiquinone oxidoreductase 15kDa subunit; CI-15 protein [Homo sapiens] >sp]O43920[NIPM HUMAN NADH-UBIQUINONE OXIDOREDUCTASE 15 KD SUBUNIT (EC 1.6.5.3) (E	catechol-O-methyltransferase [Homo sapiens] >gild03304 catechol O-methyltransferase [Homo sapiens] >pirlS3406 A38459 catechol O-methyltransferase (EC 2.1.1.6) - human >spiP21964 COMT_HUMAN CATECHOL O-METHYLTRANSFERASE; MEMBRANE-BOUND FORM (EC 2.1.1.6) (M	(AF030249) putative dienuyl-CoA isomerase [Homo sapiens] >gi 564065 peroxisomal enoyl-CoA hydratase-like protein [Homo sapiens] >pir 13882113882 peroxisomal enoyl-CoA hydratase-like protein - human >sp Q13011 ECH1_HUMAN PROBABLE PEROXISOMAL ENOYL-COA HY			
829982	830007	830019	830073	830130	830134
265	266	267	268	269	270

•					•		
Pancreas, Prostate, Breast/Ovarian	Lung, Prostate, Breast/Ovariun	Lung, Pancreus. Prostate	Lung. Pancreus	Pancreas. Breast/Overrien	Lung, Pancreus, Breast/Ovarian	Panereas, Colon	Lung. Pancreas
H2MAC06	HAICK77	H2CBC04	HYAAC49	HWLQF08	HLDCP20	HWLMF07	HWLUF58
001	79	95	100	•	001	63	
001	8Z .	95	001		001	45	
763	839	2333	1081	358	1043	1051	654
2	96	e.	7	92	m	173	\$
gi 929657	gil190247	gi 1464742	gi 3165429		piqA35569 HHMS84	gi[2315332	
neutrophil gelatinase associated lipocalin [Homo sapiens] >sp[80188]NGAL_HUMANNETROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR (NGAL) (P25) (25 KD ALPIIA-2-MICROGI,ORUI,IN-RELATIE) SUBUNIT OF MMP-9) (LIPOCALIN-2) (ONCOGENE 24P3). Length = 198	snRNP polypeptide B [Homo sapiens] >sp Q15182 Q15182 SNRNP POLYPEPTIDE B. Length = 285	threonyl-tRNA synthetase [Homo sapiens] >pir[A38867 YSHUT threoninctRNA ligase (EC 6.1.1.3) - human Length = 712	spectrin SH3 domain binding protein 1 [Homo sapiens] >sp 076049 076049 SPECTRIN SH3 DOMAIN BINDING PROTEIN 1. Length = 508		heat shock protein 84 - mouse >pirjB34461 B34461 heat shock protein 90 beta - rabbit (fragment) {SUB 1-25} >splP30947 HSSB RABIT HEAT SHOCK PROTEIN HSP 90-BETA (HSP 84) (FRAGMENT). {SUB 2-25} >pirjS13268 S13268 heat shock protein, 90K - bovine (fragment)	(AF016437) contains similarity to a C2H2-type zinc finger [Caenorhabditis elegans] >splO16350 O16350 F13H6.1 PROTEIN. Length = 631	
830135	830148	830149	830154	830183	830194	830207	830242
	272	273	274	275	276	7.72	278

			•				
Lung, Colon. Breast/Ovarian	Pancreas, Colon	Lung, Pancreas	Colon. Breast/Ovarian	Lung, Colon. Breast/Ovarian	Pancreas, Colon	Lung, Panereas. Breast/Ovarian	Lung, Colon
HWLEL26	HWLEG68	HSIA1179	нжнот21	HSUAE53	HWGQA69	HWIIPY68	HWABG32
5		001			06	901	16
≅	æ	001			06	66	
954	336	648	929	716	523	1078	6611
304	-	-	m	456	7	7	.
gi 2668505	gi 1890275	bbs 144907			gi 2443452	gi 38262	gi 180279
putative cyclin G1 interacting protein [Homo sapiens] >sp 043257 043257 PUTATIVE CYCLIN G1 INTERACTING PROTEIN. Length = 154	putative cell surface antigen [Rattus norvegicus] >splP97881 P97881 PUTATIVE CELL SURFACE ANTIGEN. Length = 547	peroxisomal acyl-coenzyme A oxidase, AOX [human, liver, Peptide, 661 aa] [Homo sapiens] Length = 661			platelet membrane glycoprotein IIIa beta subunit [Homo sapiens] >spl013495 015495 PLATELET MEMBRANE GLYCOPROTEIN IIIA BETA SUBUNIT. Length = 784	phosphate carrier protein [Homo sapiens] >pir B53737 B53737 phosphate carrier protein, form B - human Length = 361	IgG Fc receptor I [Homo sapiens] >gi[292169 Fc gamma receptor I [Homo sapiens] >pir[A39878[A39878 Fc gamma (IgG) receptor I-A (high affinity) precursor - human >spi(Q92663]Q92663 FC GAMMA RECEPTOR I. Length = 374
830328	830340	830341	830351	830358	830390	830400	830437
279	280	281	282	283	284	285	286

heparin-binding protein 15 - pig poirtJC2119JLC2119 heparin-binding protein 15 - mouse Length = 128 tenascin X [Homo sapiens] >splP78530lP78530 TENASCIN X (TENASCIN-X). >sjl2347137 (AF019413) tenascin X [Homo sapiens] {SUB 2593-4289} >pir[A42175] tenascin homolog 3.9kF3-3 - human (fragment) {SUB 2792-2880} >pir[A42175]B42175 tenascin homolog 3.9kF] carcinoembryonic antigen [Homo sapiens] gil180223 >gil 78677 carcinoembryonic antigen precursor Homo sapiens] >pir[A36319]A36319 >spl178677 carcinoembryonic antigen precursor - human -splP06731 CCEM_HUMAN CARCINOEMBRYONIC ANTIGEN PRECURSOR (CEA) (MECONIUM ANTIGEN PRECURSOR (CEA) (MECONIUM ANTIGEN PRECURSOR (CEA) (MECONIUM ANTIGEN PROCURSOR (CEA) (MECONIUM ANTIGEN PRECURSOR
80 00
renascin X [Homo sapiens] >splP78530 P7853 tenascin X [Homo sapiens] >splP78530 P7853 TENASCIN X (TENASCIN-X). >gi 2347137 (AF019413) tenascin X [Homo sapiens] {SUE 2593-4289} >pir[A42175]A42175 tenascin ho 3.9kF3-3 - human (fragment) {SUB 2793-28 >pir[B42175]B42175 tenascin homotog 3.9kF homo sapiens] >pir[A36319]A36319 carcinoembryonic antigen [Homo sapiens] >splP0673 CECM_HUMAN CARCINOEMBRYONIC ANTIGEN PRECURSOR (CEA) (MECONIUM ANTIGI 100) (CD66E carcinoembryonic antigen [Homo sapiens] >sgl 178677 carcinoembryonic antigen precurs (Thomo sapiens) >pir[A36319]A36319 carcinoembryonic antigen [Homo sapiens] >sgl 178677 carcinoembryonic antigen [Homo sapiens]

Lung, Colon, Breast/Ovarian	Lung, Pancreas, Colon	Lung, Breust/Ovarian	Lung, Pancreas	Pancreas. Prostate. Breast/Ovarian	Lung, Breast/Ovarian
111111111111111111111111111111111111111	HTLHR67	HTWJC08	нгтвнзз	HKACP86	HTPCV95
	001	001		86	
	001	901		86	28
215	733	200	377	1192	803
		m	141	~	764
	gil 1399508	gij386751		gnl PID d1000487	gi 38432
	protein kinase MUK2 [Rattus norvegicus] >gil2772514 scrinc/threonine protein kinase [Rattus norvegicus] >splP35465[PAK1_RAT SERINE/THREONINE-PROTEIN KINASE PAK- ALPHA (EC 2.7.1) (P68-PAK) (P21- ACTIVATED KINASE) (ALPHA-PAK) (PROTEIN KINASE MUK2). Length	guanine nucleotide-binding regulatory protein-beta- 2 subunit [Homo sapiens] >gi[339935 transducin beta-2 subunit [Homo sapiens] >gi[3135310 (AF033356) GNB2 [Homo sapiens] >pir[B26617]RGHUB2 GTP-binding regulatory protein beta-2 chain - human >sp[P11016]GB		(2'-5')oligoadenylate synthetase [Homo sapiens] Length = 364	P2 gene for c subunit of mitochondrial ATP synthase gene product [Homo sapiens] >gnl[PID]d1002921 ATP synthase subunit c precursor [Homo sapiens] >pir[S34067]S34067 H+transporting ATP synthase (EC 3.6.1.34) lipid-binding protein P2 precursor, mitochondri
830513	830540	830550	830567	830586	830632
292	293	294	295	296	

298	830645	propionyl CoA carboxylase beta subunit, beta PCC {EC 6.4.1.3} [human, liver, placenta, HL 1008. Peptide, 539 aa] [Homo sapiens] >pirlA53020[A53020 propionyl-CoA carboxylase (EC 6.4.1.3) beta chain precursor - human >gi]3036995 propionyl-CoA carboxylase B	bbs 140816	2 2	1505	66	66	HTEDSS8	Lung. Pancreas. Colon	
299	830652	strong homology to human RING3 sequence [Homo sapiens] >sp O60885 O60885 HUNKI MRNA. Length = 722	gnl[PLD e1290115		<i>t</i> :	3	. 4	HUKF1.74	Lung, Colon	
300	830659	CDC42 GTP-binding protein [Canis familiaris] >gil 183490 GTP-binding protein G25K [Homo sapiens] >gil293321 CDC42Mm [Mus musculus] >gil1049309 CDC42 protein [Mus musculus] >pirlA39265[A39265 GTP-binding protein G25K, placental - human >pirlS57563[S57563 CD	gij887408	<u>&</u>	714	001	001	нкаое74	Lung. Pancras. Brast/Ovarian	
301	830696	,		7	514			HSTR95	Lung. Dennet (Noneine	
302	830706			2457	2909			HELFG05	Pancrais, Breast/Overien	
303	830743	ATP SYNTHASE EPSILON CHAIN, MITOCHONDRIAL (EC 3.6.1.34). Length = 50	spIP56381 ATPE_H UMAN	æ	262	001	100	HCBBA51	Lung, Colon	
304	830770	p21-activated protein kinase [Homo sapiens] >pir SS8682 SS8682 protein kinase, p21-activated (EC 2.7.1) - human Length = 525	gi 780808	_	498	66	66	HEMCG27	Lung. Colon. Brenst/Ovarian	
305	830830	(AF002822) cyclin B2 [Homo sapiens] >sp G4101270 G4101270 CYCLIN B2. Length = 398	gi 4101270	66	1358	66	66	HROCES7	Lung, Panereas, Colon	

830838			_	747			HS2AF59	Lung, Pancreas, Colon, Breast/Ovarian
830851			7	718	į		HTX1,125	Panereas, Colon
830833			7	183			11RDDS42	Panereas, Colon
830856			542	874			HSAAX81	Coton, Breast/Ovarian
x 30862	ribosomal protein [Homo sapiens] >gi 453281 ribosomal protein S23 [Rattus norvegicus] >pir[S41955 S41955 ribosomal protein S23, cytosolie - rat >pir[S42105 S42105 ribosomal protein S23, cytosolie - human >pir[152292 152292 ribosomal protein S23 - rat >gnl	gniP1Did1603910	m	<u>8</u>	001	001	HLLCC05	f.ung. Prostate. Breast/Ovarian
830879	(AJ002120) Zfx [Monodelphis domestica] >spi019019019019 ZFX TYPE GENE (FRAGMENT). Length = 180	gniPIDle354749	7	592	39.	88	HVAAB82	Pancreas, Colon
830919			69	536			HOUHK65	Pancreas. Breast/Ovarian
830969	(AF005046) serine/threonine kinase [Homo sapiens] >gnl[PID]e1371371 (AJ011855) PAK4 protein [Homo sapiens] >sp[G4101587]G4101587 SERINE/THREONINE KINASE. Length = 591	gi 4101587	140	514	96	9 6	HOGAU20	Pancreus, Breast/Ovarian
830991	insulin-like growth factor-binding protein [Homo sapiens] >gij386791 growth factor-binding protein-3 [Homo sapiens] >gij398 (64 insulin-like growth factor binding protein 3 [Homo sapiens] >pir A36578 IOHU3 insulin-like growth factor-binding protein 3 precu	gi 183116	2	607	98	98	HDLAE73	Páncreas, Breast/Ovarian

Colon. Breast/Ovarian	Lung. Pancreas	Pancreas, Colon,	Pancreas. Colon	Lung, Pancreas	Colon, Breast/Ovarian
НОЕМ136	HAIBD64	HE8BN45	HNTSQ61	нwlес93	HNFEO67
<u>.</u> <u>00</u>	.		002	94	
	46		001	96	
974	2007	662	621	2610	928
891	16	474	-	29	755
gi 181272	pirla34789 A34789	٠	gnlPID e1363774	gi 895840	ţ
cyclin [Homo sapiens] >gi]387005 proliferating cell nuclear antigen (PCNA) [Homo sapiens] >pirA27445[WMHUET proliferating cell nuclear antigen - human >sp P12004 PCNA HUMAN PROLIFERATING CELL NUCLEAR ANTIGEN (PCNA) (CYCLIN). Length = 261	T-plastin - human >splP13797lPLST_HUMAN T-PLASTIN. {SUB 4-630} >gi190028 T-plastin polypeptide [Homo sapiens] {SUB 61-630} >gi1339848 T-plastin [Homo sapiens] {SUB 1-143} >gi1292832 T-plastin [Homo sapiens] {SUB 588-630} Lcngth = 630		(AJ006068) dTDP-D-glucose 4,6-dehydratase [Homo sapiens] >splE1363774[E1363774 DTDP-D-GLUCOSE 4,6-DEHYDRATASE (EC 4.2.1.46). Length = 350	Ip gene product [Homo sapiens] >pir S57723 S57723 Irp protein - human >sp Q 14764 MVP_HUMAN MAJOR VAULT PROTEIN (MVP) (LUNG RESISTANCE- RELATED PROTEIN). Length = 896	
831002	831003	831021	831036	831071	831094
31. 2.	316	317	318	319	320

Lung, Panereas, Colon, Breast/Ovarian	Lung. Pancreas, Colon. Breast/Ovarian	Pancreas, Colon Pancreas, Breast/Ovarian Lung, Colon	Lung. Pancreas, Colon	Pancreas. Colon. Breast/Ovarian	Panereas. Colon	ć
	Lung. I Colon. Breast/	Pancreus, Co Pancreus, Breust/Ovari Lung, Colon	Lung. Colon	Pancre	Pancre	-
HA5AB03	НМЖНР74	HWLHY12 III.WBE22 HDLAG61	HWLGP91	HMICQ42	HME1162	
001	001	99 02			6	
66	001	52			98	
1691	4 4	1221 721 829	1399	545	768	;
m	-	5 2 512	770	m	-	3
gil31442	gi 561630	gnliP1D c1349655 gil3372365			gi 207286	
fibronectin receptor beta subunit precursor (AA -20 to 778) [Homo sapiens] >pir B27079 B27079 fibronectin receptor beta chain precursor - human >sp P05556 ITB1_HUMAN FIBRONECTIN RECEPTOR BETA SUBUNIT PRECURSOR (INTEGRIN BETA-1) (CD29) (INTEGRIN VLA-4 BETA	4E-binding protein 1 [Homo sapiens] >pirJS50866[S50866 4E-BPI protein - human >pirJC5899IJC5899 initiation factor 4E-binding protein 1 - human >sp Q13541 Q13541 4E- BINDING PROTEIN 1. Length = 118	Similarity to Human hnRNP F protein (PIR Acc. No. S43484); (AF042501) cytochrome b [Homo sapiens] >sp[078829]078829 CYTOCHROME B (FRAGMENT). Length = 380			TGF-beta masking protein large subunit [Rattus norvegicus] >pir[A38261]A38261 masking protein precursor - rat Length = 1712	
831099	831113	831120 831172 831178	831184	831203	831210	921339
321	322	323 324 325	326	327	328	330

Lung. Pancreas	Pancreas, Colon	Lung, Pancreas, Colon	Pancreus. Breast/Ovarian	Lung, Colon, Breast/Ovarian	Lung, Colon
HMTBL29	нг мрооз	HUTHD56	HLQAC21	нгіссэ3	HLDNR55
94	16		<u>0</u>	66	86
94	16		001	06	86
1164	862	1310	1290	1029	1871
658	323	m	193	631	123
gi(951279	gil951279		gil186600	gni P1D d1026241	bbs 5648
MLN 64 [Homo sapiens] >dbjj D38255_1 CAB1 [Homo sapiens] >pir 138027 I38027 MLN 64 protein - human >sp Q14849 Q14849 MLN64 MRNA. Length = 445	MLN 64 [Homo sapiens] >dbj D38255_1 CAB1 [Homo sapiens] >pir 138027 138027 MLN 64 protein - human >sp Q14849 Q14849 MLN64 MRNA. Length = 445		inter-alpha-trypsin inhibitor light chain [Homo sapiens]	(AB012276) ATFx [Mus musculus] >spl070191 070191 ATFX (FRAGMENT). >splG246896 G246896 ATFX=ATF4 RELATED PROTEIN. {SUB 1-37} >splG246899 G246899 ATFX=ATF4-RELATED PROTEIN. {SUB 38-76} Length = 84	acyl coenzyme A:cholesterol acyltransferase, carboxylesterase, ACAT {EC 2.3.1.26} [human, liver, Peptide, 568 aa] [Homo sapiens] >splG415564[G415564 CARBOXYLESTERASE {EC 3.1.1.1}. {SUB 20-568} >gil719930 carboxylesterase [Homo sapiens] {SUB 62-568} Length
831256	831257	831277	831317	k 31339	831363
330	331	332	333	334	335

HI.DDR74 Lang, Colon	Lung, Panereus; Colon, Breast/Ovarian	Lung, Pancreas. Colon, Breast/Ovarian	HKGDF04 Lang, Panereus
III.DDR74	HKQAC03	HKIMC75	HKGDF04
<u>e</u>	95		ੜ
001	06		<u>ਰ</u>
8.79	383	377	1312
325	۳ .	96	254
gil 1805303	gil57064		gi[17848]
D-doparchrome tautomeruse [Homo sapiens] >gi 1864028 D-dopachrome tautomerase [Homo sapiens] >gi 3047378 (AF058293) D-dopachrome tautomerase [Homo sapiens] >gn PID e311354 phenylpyruvate tautomerase II [Homo sapiens] >gi 2352915 (AF012434) D-dopachrome ta	cDNA from hypercalcemic tumour [Rattus norvegicus] >pirl\$28223 \$28223 parathyroid hormone-like protein - rat >sp Q05310 L10K_RAT LEYDIG CELL TUMOR 10 KD PROTEIN. Length = 93	•	aldehyde reductase (EC 1.1.1.2) [Homo supiens] >gi 2707824 (AF036683) aldehyde reductase [Homo sapiens] >pir A33851 A33851 alcohol dehydrogenase (NADP+) (EC 1.1.1.2) - human >spi G2707824 G2707824 ALDEHYDE REDUCTASE. >sp P14550 ALDX_HUMAN ALCOHOL DEHYDROGE
831367	831379	831385	831390

340	831391	islet regenerating protein [Homo sapiens] >pir[A35197]RGHU1A regenerating islet lectin 1- alpha precursor - human >splP05451 LITA_HUMAN LITHOSTATHINE 1 A1.PIIA PRECURSOR (PANCREATIC STONE PROTEIN) (PSIY) (PANCREATIC THREAD PROTEIN) (PTP) (ISLET OF LANGERHANS	gil 190979	12	592		001	Н LDB606	Panereas, Colon	
341	831405	factor H homologue [Homo sapiens] >pir[156100[156100 factor H homologue - human >sp[Q03591]CFH1_HUMAN COMPLEMENT FACTOR H-LIKE PROTEIN I PRECURSOR (H36). Length = 330	gi 183763	53	1078	94	94	нгровзт	Lung. Panereas. Colon, Breast/Ovarian	
342	831442	PDGF associated protein [Homo sapions] >splQ13442[HP28_HUMAN 28 KD HEAT- AND ACID-STABLE PHOSPHOPROTEIN (HASPP28) (PDGF ASSOCIATED PROTEIN). Length = 181	gi 1136584	7	595	09	09	HKAEBIS	Lung. Pancreas. Colon. Breast/Ovarian	
343	831476	dermatopontin [Homo sapiens] -pir[A47220]A47220 dermatopontin precursor - human -sp[Q07507]DERM HUMAN DERMATOPONTIN PRECURSORpir[S34838[S34838 tyrosine-rich acidic matrix protein - pig {SUB 101-144} Length = 201	gi311614	_	630	16	16	Н)МВК21	Lung. Panereas. Colon	
344	831488	similar to Saccharomyces cerevisiae Spt4; protein has potential N-terminal zinc-finger [Homo sapiens] >gil 401053 SUPT4H [Homo sapiens] >gil 401053 SUPT4H [Homo sapiens] >gil 401065 Supth [Mus musculus] >gil3779194 chromatin structural protein homolog [M	gil1209779		580	001	. 001	HJBCG39	Colon. Breast/Ovarian	

!									
345	831518			240	467			HATCV09	Pancreas, Coton. Breast/Ovarian
346	831519	(AF062536) cullin 1 [Homo sapiens] >splO60719(O60719 CULLIN 1. >gi 4153866 (AC005229) cullin 1 [Homo sapiens] {SUB 1-263} Length = 776	gi3139077	165	1712	001	. 001	ПОЕСИ	Pancreas. Breast/Ovarian
347	831521			m	863			HIBCE91	Colon. Breast/Ovarian
348	831550	mel-13a protein - mouse Length = 132	. pirlS65785 S65785	158	457	. 02	75	HCHNH46	Lung, Pancreas, Breast/Ovarian
349	831560			1474	1818			HCROA68	Pancreas. Breast/Ovarian
350	831562	fibromodulin [Homo sapiens] >splQ06828 FMOD_HUMAN FIBROMODULIN PRECURSOR (FM) (COLLAGEN-BINDING 59 KD PROTEIN). Length = 376	gi[297091		1272	06	91	HEGAD80	Pancreas. Breast/Ovarian
351	831570	(AF042822) epithin [Mus musculus] >splG4104970 G4104970 EPITHIN Length = 902	8i 4104970	7	1861	11	. 82	HI.WCC68	Lung, Panerens, Colon
352	831593			726	878			HHBFW28	Lung, Pancreas
353	831596	32 kd accessory protein [Bos taurus] >gi 190376 proton ATPase accessory subunit [Homo sapiens] {SUB 264-351} Length = 351	gi 736727	7	808	001	100	нчерл61	Colon. Breast/Ovarian
354	831627		٠.,	-	903			HBJH146	Lung. Pancreas
355	831649			-	738			HFTDD09	f.ung. Colon
356	831664	transformation upregulated nuclear protein - human pir S43363 S43363 Length = 464	pirJS43363JS43363	180	1574	2 6	94	HFPCU40	Lung. Colon

Panereas, Colon	Panerens. Colon	Panereas, Colon	Lung. Breast/Ovarian	Colon. Breast/Ovarian	Pancreas. Colon	Lung, Pancreus, Breast/Ovarian
Panere	Panere	Panere	Lung. Breast/	Colon.	Pancre	Lung. I Breast/
HĽDOX36	HFOXE22	HFKHD75	HAGDQ%	HLWEQ18	HEOBI79	НКАНВ85
96	96	%	86			11
96	96	5 .	86			92
1338	1311	30\$	454	484	720	812
-	-	. 09	1.	95	37	m
gi 179720	gi 2997692	09790	gi 312345			gij31065
complement protein C8 beta subunit precursor [Homo sapiens] >pirJA43071[C8HUB complement C8 beta chain precursor - human >splP07358[C08B_HUMAN COMPLEMENT COMPONENT C8 BETA CITAIN PRECURSOR. Length = 591	(AF033630) monocyte/neutrophil elastase inhibitor [Homo sapiens] >pirJS27383/S27383 elastase inhibitor - human >splP30740 LEU_HUMAN LEUKOCYTE ELASTASE INHIBITOR (LEI) (MONOCYTENEUTROPHIL ELASTASE INHIBITOR) (EI) >splG2997692 G2997692 MONOCYTE/NEUTROPHI	Mpv 17 [Mus musculus] >pir[\$29031 \$29031 mpv 17 protein - mouse >sp[P19258 MPV1_MOUSE MPV 17 PROTEIN >gi]3252875 (AF038632) Mpv 17 protein [Mus musculus] {\$UB 155-176} Length = 176	rat ribosomal protein L36 [Rattus norvegicus] >pirJN0483JN0483 ribosomal protein L36 - rat Length = 105			ear-2 gene product [Homo sapiens] >pir S02709 S02709 ear-2 protein - human >sp P10588 EAR2_HUMAN V-ERBA RELATED PROTEIN EAR-2. Length = 403
831674	831684	831687	831726	831736	831762	831801
357	358	359	360	361	362	363

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Lung, Colon, Breast/Ovarian	Lung. Panereas. Breast/Ovarian	Lung. Colon	Colon, Breast/Ovarian	Colon. Breast/Ovarian	Lung, Colon	Lung, Panereas, Breast/Ovarian	Lung, Pancreas, Colon, Breast/Ovarian	Panereas, Colon. Breast/Ovarian	Lung, Panereas. Colon
HE8AF82	HJPCX51	HE6FG90	HDTLN67	HDTBQ51	HLYGA31	HDPKK57	HDPFP36	1101101168	HDFUB44
	77	1001			76	88			69
	E	001			96	33			57
2284	377	1186	199	693	1132	855	802	467	348
2018	341	53	7	- .	\$6	331	425	30	
	gil3986442	gi 3341992			gi 1825562	gi 1477565			gnl PiD e1293199
	(AF076786) serum amyloid A-activating factor SAF-8 [Oryctolagus cuniculus] >-spk(33986442[c;3986442 SERUM AMYLOH) A-ACTIVATING FACTIOR SAF-8 (FRAGMENT). Length = 214	(AF054174) histone macroH2A1.2 [Homo sapiens] >sp G3341992 G3341992 HISTONE MACROH2A1.2. Length = 371			nuclear antigen H731 [Homo sapiens] >pirJC5193JJC5193 nuclear protein H731 - human >sp[Q99834[Q99834 NUCLEAR ANTIGEN H731.	p619 [Homo sapiens] >pir S71752 S71752 giant - protein p619 - human >sp Q15751 Q15751 P619. Length = 4861			(AL021918) b3418.1 (Kruppel related Zinc Finger protein 184) [Homo sapiens] >spl060792/060792 B3418.1 (KRUPPEL RELATED ZINC FINGER PROTEIN 184). Length = 751
831848	831861	831866	831878	831899	831913	831972	831985	831986	832010
364	365	366	367	368	369	370	37.	372	373

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Lung. Breast/Ovarian	Lung, Pancreas, Colon	Lung. Panereas. Colon, Breast/Ovarian	Lung, Pancreas, Breast/Ovarian	Lung, Pancreas. Colon, Breast/Ovarian	Colon. Breast/Ovarian	Pancreas. Breast/Ovarian	Lung, Coton Lung, Panereus
Lung. Brenst	Lung. Coton	Lung. I Colon, Breast/	Lung. Breast	Lung. I Colon. Breast/	Colon. Breast/	Pancreas. Breast/Ov	Lung. Colon Lung, Panere
HT/DG34	HDPGC33	HGCOL40	HCFAU68	HCUDT18	HEHN81	IICQAIISI	HOCTE23 HCMSD61
H	HDP	IIGC	HCF	нсп	H	021	HOCH
001	901	66	901				
×	=	≎	2				
100	001.	66	66				
604	1472	1794	710	846	380	642	553 959
				_			_
7	\$	-	%	427	246	433	290
£	pir A49499 A49499)12226	06190				
gi 37543	149499	<u>բոլ PID d1012226</u>	gnIPIDId 1 006 1 90				
	pirk	lng	ll us				
[Homo sapiens] JI snRNP protein C - human	(EC 3.4.24) - human IUMAN MACROPHAGE SE PRECURSOR (EC ATRIX ASE-12) (MMP-12). Length	5-aminoimidazole-4-carboxamide-1-beta-D- ribonucl eotide transformylase/inosinicase [Homo sapiens] >gn PID d1022617 5-aminoimidazole-4- carboxamide ribonucleotide transformylase [Homo sapiens] >pir JC4642 JC4642 purH bifunctional enzyme - human >sp Q13856	proteasome subunit HsC10-II [Homo sapiens] >pirJS504 IS5504 multicatalytic endopeptidase complex (EC 3.4.99.46) beta chain C10-II - human >spiP49720 PRCT_HUMAN PROTEASOME THETA CHAIN (EC 3.4.99.46) (MACROPAIN THETA CHAIN) (MULTICATALYTIC ENDOPEPTIDASE C				
ens] rotein C	(EC 3.4.24) - human IUMAN MACROPHAGE SE PRECURSOR (EC ATRIX IASE-12) (MMP-12). Leng	-I-beta- ssinicase inoimid formylas formylas	mo sapi n C10-II)TEASC MACIRC LYTIC				
[Homo sapiens] J1 snRNP protei	3.4.24 (AN M/ RECUR (IX E-12) (N	oxamide rlase/ino 17 5-am de transf 542 purf 856	0-11 [Ho icatalytiv eta chaii AN PRC 99.46) (i				
59) [Ho 87 U1 sı	ME (EC 3.4 MENDAN MENDE PRECENTIX MATRIX EINASE-12	4-curboxan nsformylass nsformylass ncleotide tr nglQ13856l splQ13856l	ir HsC11 41 multi 99.46) b 9.46) b 1 HUM, EC 3.4.5 (MULT				
(AA 1-1 87 S013 159	stase Hi OlCOGN OELAS (HME) OPROT	nidazole otide tra gn[PID] de ribor pir[JC46	e subun HISS50 EC 3.4.5 OPRCT HAIN (HAIN)				
C protein (AA 1-159) >pir S01387 S01387 L Length = 159	metalloelastase HME (EC 3.4.24.) - human >spil/39900 COGM_HUMAN MACROPHAMETALLOELASTASE PRECURSOR (EC 3.4.24.65) (HME) (MATRIX METALLOPROTEINASE-12) (MMP-12), 1 = 470	5-aminoimidazole-4-carboxamide-1-beta-D-ribonucl eotide transformylase/inosinicase [Horsapiens] >gnl[PID]d1022617 5-aminoimidazole carboxamide ribonucleotide transformylase [Hosapiens] >pir[JC4642]C4642 purH bifunctional enzyme - human >sp[Q13856]	proteasome subunit HsC10-II [Homo sapiens] >pirJS55041 S55041 multicatalytic endopeptidase complex (EC 3.4.99.46) beta chain C10-II - huma >spiP49720 PRCT_HUMAN PROTEASOME T11ETA CHAIN (EC 3.4.99.46) (MACROPAIN THETA CHAIN) (MULTICATALYTIC ENDOPEPTIDASE C				
					•	_	
832016	832041	832044	832049	832122	832148	832197	832237 832246
374	375	376	37.7	378	379	380	381 382
• •	• •	• •	• •	• • •		•••	,

392	832394	platelet-endothelial tetruspan antigen 3 [Homo sapiens] > splP48509(C151_HUMAN PLATELET-ENDOTHELIAL TETRASPAN ANTIGEN 3 (PETA-3) (GP27) (MEMBRANE GLYCOPROTEIN SFA-I) (CD151 ANTIGEN). Length = 253	gi 541613	C1	847	.	%	HETTID21	Lung, Pamerreas
393	832454	precursor polypeptide [Homo sapiens] >pir A25971 C2HU complement C2 precursor - human >gi 187765 MHC complement component C2 [Homo sapiens] {SUB 21-46} Length = 752	gi 34628	160	357	001	. 001	HLQBT44	Prostate. Breast/Ovarian
394 395	832465	X box binding protein-1 [Homo sapiens]	gi 306893	1 470	324	00	. 00	HAJBC51 HTJMJ52	Lung. Pancreas Pancreas.
396	832495	>pirlA36299 A36299 transcription factor hXBP-1 - human Length = 260 FR1 Homo canions > pirl 52726 FR1 -	1,1008357	-	933	9	9	780C1711	Breast/Ovarian
3		human >sp[Q15691[Q15691 EB1. Length = 268	S(7007)		CC.	}		Coccine	ניוווק. ניוורניוא
397	x32498	pyrrolinc-5-carboxylate synthase [Homo sapiens] >spjG4097816jG4097816 PYRROLINE-5- CARBOXYLATE SYNTHASE, Length = 793	gj 4097816	6 1	1036	95	95	HLTGQ24	Lung, Panereas
398	832501			736	966			HAGF157	Lung, Pancreas, Colon
	832505	protein synthesis factor [Homo sapiens] >spjP47813 IF1A_HUMAN EUKARYOTIC TRANSLATION INITIATION FACTOR IA (EIF- IA) (EIF-4C). {SUB 2-144} Length = 144	gi 306725	1 9	648	001	001	HRABV57	Lung, Pancreas. Prostate
400	832539	protein synthesis initiation factor 4A [Mus musculus] Length = 408	gi 673433	472	1125	. 60	93	HRABO69	Lung. Breast/Ovarian
401	832554	HSGCN1 [Homo supiens] >sp[Q99736][Q99736] HSGCN1 (FRACIMENT). Length = 1928	<u>હા</u>]2282576	409	927	66	66	HCHOX71	Panereus. Breust/Ovarian

ë u	s	. .	£	5	: 4 =	ý =
Lung. Colon Panereus. Colon. Breast/Ovarian	Lung, Colon Colon, Brenst/Overrin	Lung. Colon. Breast/Ovarian	Pancreus. Breast/Ovarian	Lung. Remett tearing	Lung. Pancreas. Colon. Breast/Ovarian	Lung, Pancreas, Colon, Breast/Ovarian
HFCAE43 HBBBD67	H2CBK94 H2CBG53	H2CBD94	HWACF51	HCPCK33	HHBE126	HSTA170
3		69	2		. 65	001
		23	32		4	66
956	992	592	999	604	1431	541
.2	630	-	m	7	634	53
gni PID e1295805		gi 2344898	gi 466475		gij1123105	hbs 174416
(AL023777) rna binding protein [Schizosaccharomyces pombe] >sp 074978 074978 RNA BINDING PROTIEIN. I.cngih = 276		(AC002388) 60S ribosomal protein L30 isolog [Arabidopsis thaliana] >splO22165 022165 60S RIBOSOMAL PROTEIN L30 ISOLOG. Length = 159	putative phospho-beta-glucosidase [Bacillus stearothermophilus] > pir[D49898]D49898 cellobiose phosphotransferase system celC - Bacillus stearothermophilus > sp[Q45401]Q45401 PUTATIVE PHOSPHO-BETA-GLUCOSIDASE. Length = 245		similar to S. cerevisiae longevity-assurance protein 1 (SP:P38703) [Caenorhabditis elegans] >sp[Q17870[Q17870 SIMILAR TO S. CEREVISIAE LONGEVITY-ASSURANCE PROTEIN 1. Length = 362	acidic calponin [human, kidney, Peptide, 329 aa] [Homo sapiens] >pir JC450 JC450 acidic calponin - human >sp Q 5417 Q 5417 ACIDIC CALPONIN, Length = 329
832569 832578	832615 832620	832632	832633	833483	834574	834859
402	404	406	407	408	409	410

11	834861	factor activating exoenzyme S [Bos taurus] >gil189953 phospholipase A2 [Homo sapiens] >gil899459 14-3-3 protein [Homo sapiens] >pirA38246[PSHUAM 14-3-3 protein zeta - human >pirA47389[A47389 14-3-3 protein zeta - howine >spiP29312[143Z_HUMAN 14-3-3 PROT	gi 163042	74	967	66	6	HBXFL41	Lung, Pancreas. Prosinte. Breast/Ovarian
412	8,14890	TRANSCRIPTION FACTOR BIT3 (RNA POLYMERASE B TRANSCRIPTION FACTOR 3), Length = 204	splQ64152 BTF3_M OUSE	70	888.	06	16	112CBT12	Lang, Panereas. Prostate. Breast/Ovarian
413	835079			151	348			ноегн62	Lung, Panerens,
414	X35554	homologue to sec61 [Rattus rattus] Length = 476	gi 206886	121	1287	86	86	нонвн04	Lung, Pancreas
415	835560			C1	574			HE9NK60	Lune, Panereas
416	835723	immunoglobulin M heavy chain [Homo sapiens] >g]8408 immunoglobulin M heavy chain [Homo sapiens] >pir[S37768 S37768 Ig mu chain C region human Length = 453	gi 38406	. ∞	1421	001	100	HLYFY90	Lung. Pancreas. Prostate. Colon. Breast/Ovarian
417	835791	(AJ005890) JM1 [Homo sapiens] >splO60826[O60826 JM1 PROTEIN, COMPLETE CDS (CLONE LLNLC110M0111Q7 (RZPD BERLIN)AND LI.NLC110K2140Q7 (RZPD BERLIN). Length = 627	gni PID c1289743	437	1177	87	87	HTYJH25	Pancreas. Breast/Ovarian
418	835817			1369	1554			HAJAZ17	Lung.
419	835840 836048			2 2052	730 2276			ннеол47 проругі	Dreascovarian Lung, Pancreas Lung, Prostate

421	836898	human P5 [Homo sapiens] >pirJC4369JC4369 P5 protein - human >splQ15084JERP5_HUMAN PROBABLE PROTEIN DISULFIDE ISOMERASE P5 PRECURSOR (EC 5.3.4.1). Length = 440	1906011plq100501	en .	1427	06	06	HWIIPA75	Lung, Panereas. Colon. Breast/Overian
422	K36927	(AF027299) protein 4.1-G [Homo sapiens] >sp O43491 O43491 PROTEIN 4.1-G. Length = 1005	gil2739096	e.	9611	₹ ∞	%	11DTKY58	Lung, Panereas
423	837344	SIR [Cowpox virus] >splO72763 O72763 SIR PROTEIN. Length = 210	gni P1D c1289272	88	658	8	28	HLDAG32	Lung, Prostate
424	837789	bikunin [Homo sapiens] >spl000271 000271 BIKUNIN. Length = 252	gi 2065529	365	1231	16	16	HDABR73	Colon. Breast/Ovarian
425	838549	(AL.023828) Y17G7B.14 [Caenorhabditis elegans] >splE1323274 E1323274 Y17G7B.14 PROTEIN. Length = 364	gnl P1D e1323274	2	853	42	55	HDQDW\$6	Lung. Breast/Ovarian
426	838754	,		. 437	8611			HTEQK83	Lung, Panereas, Breast/Ovarian
427	838768			570	770			HWBCW80	Lung, Panereas, Breast/Ovarian
428	K39486	fibronectin precursor [Homo sapiens] >gil4096846 fibronectin [Homo sapiens] {SUB 76-454} >gil4096848 fibronectin [Homo sapiens] {SUB 1892-2103} >gil182706 fibronectin [Homo sapiens] {SUB 1921-2040} >gil182684 fibronectin [Homo sapiens] {SUB 2233-2328} Len	gil31397	7	493	86	86	HSI.GC71	Lung. Breust/Ovarian
429	839561	p34 protein [Rattus sp.] >pirlS36779 S36779 ribosome-binding protein p34 • rat >splQ63742 Q63742 P34 PROTEIN. Length = 307	gnilP1D d1003291	45	1133	98	<u>∞</u> ∞	HUVFB27	Lung, Panereas, Prostate

Lung. Breast/Ovarian	Lung, Pancreas. Breast/Ovarian	Lung, Pancreas	Lung, Panerens
HWADY II Lia	НЕВЕН64 Lu	HSRBI81 Lu	HOEMS29 La
1 9	8		001
9	7.6	93	001
432	757	1493	1370
- .	7	219	1038
sil1293808	gni PID d1006692	gil3152835	gi 180924
similar to plasmodium merozite surface antigen precursor (SP:P04933) [Caenorhabditis elegans] >sp[Q22585[Q22585 SIMILAR TO PLASMODIUM MEROZITE SURFACE ANTICIEN PRECURSOR. Length = 634	UMP-CMP kinase [Sus scrofa] >pirlJC4181JJC4181 cytidylate kinase (EC 2.7.4.14) - pig >sp[Q29561JKCY_PIG UMP-CMP KINASE (EC 2.7.4.14) (CYTIDYLATE KINASE) (DEOXYCYTIDYLATE KINASE). Length = 196	(AF062328) p120 catenin isoform 1AB [Homo sapiens] >sp[060715 060715 P120 CATENIN ISOFORMS 1AB, 2AB, 3AB AND 4AB. >gi[3152823 (AF062322) p120 catenin isoform 2AB [Homo sapiens] {SUB 55-962} >gi[3152855 (AF062338) p120 catenin isoform 3AB [Homo sapiens] {S	connective tissue growth factor [Homo sapiens] >gi474934 connective tissue growth factor [Homo sapiens] >pir/A40551 A40551 connective tissue growth factor - human >splP29279 CTGF_HUMAN CONNECTIVE TISSUE GROWTH FACTOR PRECURSOR, >gi 984956 connective tiss
839816	840068	840279	840489
430	431	432	433

Lung, Pancreas. Prostate, Breast/Ovarian	Lung, Panereas. Colon. Breast/Ovarian	Lung, Prostate	Lung, Prostate, Colon	Prostate, Colon	Lung. Pancreas. Prostate. Colon. Breast/Ovarian	Lung, Pancreas. Prostate, Colon	Lung, Panereas
HYAAN81	HMCFK75	HWHGB33	HWLKM77	H6EDS19	HLIB207	HSSDI65	HPJDB01
			93		22	96	89
. 001			93		2	96	67
2298	1302	492	1409	1014	495	1476	889
· —	145	-	m	346		103	2
gni P1D d1006904			gni P1D d1020288		gi 51442	हां2589011	gi 929660
glycyl tRNA synthetase [Homo sapiens] >pirlA55314[A55314 glycinetRNA ligase (EC 6.1.1.14) precursor - human >gi 600727 glycyl- tRNA synthetase [Homo sapiens] {5UB 55-739} >gi 3845409 (AC004976) glycyl tRNA synthetase [Homo sapiens] {5UB 348-739} Length ==			IgG Fc binding protein [Homo sapiens] Length = 5405		putative [Mus musculus] >pirJS15785JS15785 heatstable antigen-related hypothetical protein HSA-Comouse >sp[Q61692[Q61692 HSA-C GENE CODING FOR HEAT STABLE ANTIGEN Length = 141	(AB008549) type 1 procollagen C-proteinasc enhancer protein [Homo sapiens] >gil3135316 (AF053356) PCOLCE [Homo sapiens] >spl014550[014550 TYPE 1 PROCOLLAGEN C- PROTEINASE ENHANCER PROTEIN. Length = 449	PQ-rich protein [Homo sapiens] >pir[SS8222 SS8222 PQ-rich protein - human >spiQ15184 Q15184 PQ-RICH PROTEIN. Length = 400
840538	840545	840549	840551	840557	840561	840562	840564
434	435	436	437	438	439	440	441

442	840572	putative [Homo sapiens] >pirl154339 154339 protoncogene - human >sp P35226 BMII_HUMAN DNA-BINDING PROTEIN BMI-I. Length = 326	gi 291873	m	1172	95	8	HTGAZ34	Prostate, Colon	
443	840600			m	611			HYABI30	Prostate. Breast/Ovarian	
444	840604	Similarity to Mouse A-RAF proto-oncogene serinc/throonine-protein kinase (SW:KRAA_MOUSE);	gni PIDje1344589		1359	82	87	HWI.HN58	Lung, Panereas. Prostate. Breast/Ovarian	
445	840608	ollictomedin [Rana catesbeiana] -pirjA4742[A4742 olfactomedin precursor - bullfrog -sp[Q07081[OLFM RANCA OLFACTOMEDIN PRECURSOR (OLFACTORY MUCUS PROTEIN). Length = 464	Bi 294502	200	1549	55	75	HWLFY46	Panereas, Colon	
446	840620			776	1267			HTXGB37	Lung. Prostate	
447	840625			138	257	٠		HTXDT74	Lung. Prostate	
4 4 8	840626	nicotinamide N-methyltransferase [Homo sapiens] >gil1063610 nicotinamide N-methyltransferase [Homo sapiens] >pirlA54060[A54060 nicotinamide N-methyltransferase (EC 2.1.1.1) - human >splP40261[NNMT_HUMAN NICOTINAMIDE N-METHYLTRANSFERASE (EC 2.1.1.1). Lengt	gi 494989	485	1282	100	001	HULAS90	Lung, Pancreas. Prostate. Colon. Breast/Ovarian	
449	840638			91	.351			HTTDV02	Prostate.	
450	840649	BL34=B cell activation gene [human, Peptide, 196 aa] [Homo sapiens] >pir[156165 156165 B cell activation protein BL34 - human Length = 196	bbs 129951	_	651	.001	100	HTWCY84	Dicabrovanian Lung, Prostate	
451	840651			7	706			H1TAD76	Pancreas. Prostate	

452	840666		•	7	826			HTOAF86	Lung, Prostate
453	840681			157	2187			HTAER63	Lung, Prostate
454	840682	siah binding protein 1 [Homo sapiens]. >sp Q99628 Q99628 SIAH BINDING PROTEIN 1 (FRAGMENT). Length = 541	gi 1809248	_	1734	66	66	HE9PW64	Lung. Breast/Ovarian
455	840684			m	539			HTGB/F14	Panercas. Prostate. Breast/Ovarian
456	840697			96	999			HTECA 52	Lung, Prostate
457	840698	t-complex-type molecular chaperone TCP1 - human >gij339211 t-complex 1 protein [Homo sapiens] {SUB 308-365} Length = 556	pir S10486 S10486	507	1853	%	97	HDABW50	Pancreas. Prostate
458	840708			1200	1487			HTEAF73	Lung, Prostate
	840714	(AF053304) mitotic checkpoint component Bub3 [Homo sapiens] >gi[2921873 (AF047472) spleen mitotic checkpoint BUB3 [Homo sapiens] >gi[3639060 (AF081496) kinetochore protein BUB3 [Homo sapiens] >sp[043684[043684 SPLEEN MITOTIC CHECKPOINT BUB3. Length = 328	gil2981231		1170	001	001	HTEGU90	Lung, Pancreas, Prostate, Breast/Ovarian
460	840716	(AC005326) asparagine synthetase [Homo sapiens] >sp[G3341715 G3341715 ASPARAGINE SYNTHETASE. >gi[703119 asparagine synthetase [Homo sapiens] {SUB 1-83} Length = 561	gi3341715	991			94	HSYAJ64	Lung, Prostate. Colon. Breast/Ovarian
461	840721			7	1324			HSUSE92	Lung, Puncrens, Prostate, Colon

840735	(AC002425) Gene product with similarity to Rat P8 [Homo sapiens] >gi]3202004 (AF069073) P8 protein [Homo sapiens] >gi]3202006 (AF069074) P8 protein [Homo sapiens] >sp[O60356[O60356 Ci]:NI; PRODUCT WITH SIMIL ARITY TO RAT	gil2947054	Ξ	392	1 9	49	HSRON44	Lung, Panereus. Prostate. Breast/Ovarian
840738			882	1230			IFTOJKII	Prostate, Colon
840745	52-kD SS-A/Ro autoantigen [Homo sapiens] Length = 475	gi 338490	7	694	46	63	HSSGC06	Lung, Prostate, Colon
840747	(AC004522) Zn-alpha2-glycoprotein [Homo sapiens] >splO60386 O60386 ZN-ALPHA2-GLYCOPROTEIN. Length = 334	gi 3006228	368	877	. 56	95	HLDOL02	Lung, Panereas, Breast/Ovarian
840756	(AB005624) rig-analog DNA-binding protein [Sus scrofa] >gi]306898 rig-analog protein (putative); putative [Homo sapiens] >gi]37416 human homologue of rat insulinoma gene (rig); putative [Homo sapiens] >gi]305361 Rig DNA-binding protein (putative); putati	gni[P1D]d1022359	2	480	76	76	нснвозз	Lung, Pancreas. Colon. Breast/Ovarian
840776	Notch3 [Homo sapiens] >splG2668592 G2668592 NOTCH3. Length = 2321	gi 2668592		364	82	83	HSKJZ22	Lung. Breast/Ovarian
840784	aldehyde dehydrogenase 6 [Homo sapiens] >pir A55684 A55684 aldehyde dehydrogenase (NAD+) (EC 1.2.1.3) 6 precursor, salivary - human >sp P47895 DHA6_HUMAN ALDEHYDE DEHYDROGENASE 6 (EC 1.2.1.5) Length = 512	gi 544482	-	9 .	₹6	56	HSKAC75	Lung, Prostate, Colon, Breast/Ovarian

 73 .

469	840788	P1 gene for c subunit of human mitochondrial ATP synthase gene product [Homo sapiens] >gn][P1D]d1002920 ATP synthase subunit c precursor [Homo sapiens] >pir/S34066[S34066 H+transporting ATP synthase (EC 3.6.1.34) lipidbinding protein P1 precursor, mitoc	gij38430	59	484	\$8	%	нн Гим 32	Lung, Prostate, Colon. Breast/Ovarian	
470	840794			162	1646			HOHB128	Lung, Panereus,	
471	840797	OSF-2p1 [Homo sapiens] >pir S36111 S36111 osteoblast-specific factor 2 - human >sp Q15064 Q15064 OSF-2P1. Length = 779	gni P1D d1003341	2	2371	93	6	HDTIM52	Prosane. Colon Pancreas. Breast/Ovarian	
472	840799		·	292	\$10	•		HWBC148	Lung, Puncreas, Colon, Breast/Ovarian	
473	840818	translational initiation factor eIF-2, alpha subunit [Homo sapiens] >splP05198[IF2A_HUMAN EUKARYOTIC TRANSLATION INITIATION FACTOR 2 ALPHA SUBUNIT (EIF-2- ALPHA). {SUB 2-315} Length = 315	gi 181995	m	908	001	001	нивнм68	Lung. Prostate	
474	840822	fatty acid synthase [Homo sapiens] -pir[G01880 G01880 fatty-acid synthase (EC 2.3.1.85) - human -sp[Q16702 Q16702 FATTY ACID SYNTHASE (EC 2.3.1.85) (FATTY-ACID SYNTHASE). Length = 2509	gi[915392	1423	2367	93	æ	HCBHX28	Lung. Prestate. Colon. Breast/Ovarian	
475	840830	diubiquitin [Homo sapiens] >spl015205 015205 DIUBIQUITIN. Length = 165	gnl PID e321293	-	573	66	8	HFXHP85	Panereas. Prostate	

glutathione S-transferase Ha subunit 1 (EC 2.5.1.18) gij306810 144 [Homo sapiens] >gij306815 glutathione S- transferase (GST, EC 2.5.1.18) [Homo sapiens] >gij306809 glutathione S-transferase [Homo sapiens] >bbs/76373 glutathione S-transferase Hal subunit {EC 2.5.1.18} [prohibitin [human, Peptide, 272 aa] [Homo supiens] bbs 85658 81 >pir 152690 152690 prohibitin - human >sp P35232 PHB_HUMAN PROHIBITIN. Length = 272	NAP [Homo sapiens] >pir S40510 S40510 gi 189067 92 nucleosome assembly protein 1-like 1 - human >spiP55209 NPL I_HUMAN NUCLEOSOME ASSEMBLY PROTEIN 1-LIKE 1 (NAP-1 RELATED PROTEIN). Length = 391	(AL021546) Cytochrome C Oxidase Polypeptide gnl PID e1248288 2 VIa-liver precursor (EC 1.9.3.1) [Homo sapiens] >sp O43714 O43714 CYTOCHROME C OXIDASE POLYPEPTIDE VIA-LIVER PRECURSOR (EC 1.9.3.1) (CYTOCHROME-C OXIDASE) (CYTOCHROME OXIDASE) (CYTOCHROME A(3)) (CYTOCHROME AA(3)	DNA polymerase delta small subunit [Homo gi 1008458 2 sapiens] >pir 138950 138950 on A-directed DNA polymerase (EC 2.7.7.7) delta regulatory chain - polymerase (EC 2.7.7.7) delta regulatory chain - polymerase (EC 2.7.7.7) EL SMALL SUBUNIT (EC 2.7.7.7). Length = 469
				1008458 2
		1309		' 9
833 95	917 93	99 80	520 100	658 69
\$6	93	08	001	66
Н ГУНР57	1111B11M75	HDTL_J39	HFPBO29	HSDIX61
Prostate. Brenst/Ovarian	Lung, Panereas, Prostate, Breast/Ovarian	Lung, Pancreas, Colon, Breast/Ovarian	Lung. Prostate, Breast/Ovarian	Pancreas, Colon. Breast/Ovarian

478

477

28

HPTDK64 Lung, Prostate	Lung, Panereas. Colon, Breast/Ovarian	Prostate, Colon, Breast/Ovarian	Lung. Prostate	Panerens. Prostate	Lung, Panereas, Prostate	Lung, Prostate	Pancreas. Breast/Ovarian
HITDK64	H2MBT19	HFIXK16	нвснія	HETAD58	HEOMT66	HF1BB89	HCHNJ32
46	001		66			.	76
3	8		86			93	19
873	929	320	1565	366	1347	1675	878
_	227	153	108	103	92	2	277
gi 337999	gni P1D d1006216		gi 1458228			gi 179281	gni PID d1004479
secreted cyclophilin-like protein [Homo sapiens] >gi 81335 cyclophilin B [Homo sapiens] {SUB 9-216} >gi 181250 cyclophilin [Homo sapiens] {SUB 10-216} Length = 216	unknown [Homo sapiens] >sp P41271 DAN_HUMAN ZINC FINGER PROTEIN DAN (N03). Length = 180		mutY homolog [Homo sapiens] >sp[Q15830]Q15830 MUTY HOMOLOG. Length = 535			ATP synthase beta subunit precursor [Homo sapiens] >pirJA33370JA33370 H+-transporting ATP synthuse (EC 3.6.1.34) beta chain precursor. mitochondrial - human >splP06576JATPB_HUMAN_ATP_SYNTHASE_BETA_CHAIN, MITOCHONDRIAL_PRECURSOR (EC 3.6.1.34). >gi[28931 be]	carbonyl reductase [Sus scrofa] >pirJN0703JN0703 carbonyl reductase (NADPH) (EC 1.1.1.184) - pig >splQ29529 CBR2_PIG LUNG CARBONYL REDUCTASE [NADPH] (EC 1.1.184) (NADPH-DEPENDENT CARBONYL REDUCTASE) (LCR). Length = 244
840874	840878	840880	840884	840907	840926	840932	840940

489	840947			7	. \$9\$		٠	HEGAN45	Lung, Panereas, Prostate, Breast/Ovarian
490	840959	signal peptidase complex 25 kDa subunit Canis familiaris >pirlA55012 A55012 signal peptidase 25k chain - dog Length = 226	gi 533111	Ci	712	8	66	HEDAD\$3	Lang, Panereas, Prostate, Breast/Ovarian
491	840964			177	344			HERUK92	Prostate, Colon
492	840979	transcription factor-like protein 4 - human Length = 298	pirJC5333JC5333	=	631	66	100	HE9HD45	Lung, Pancreas. Prostate, Colon
493	840984	p167 [Homo sapiens] >gnt PID d1010130 The KIAA0139 gene product is related to mouse centrosomin B. [Homo sapiens] >gi 2501783 translation initiation factor 3 large subunit [Homo sapiens] >sp Q14152[Q14152 KIAA0139 PROTEIN - >gi 1399801 p167 [Homo sapiens]	gi 1808985	m	3017	16		HE8OC40	Lung, Pancreas. Prostate, Breast/Ovarian
					-				
494	840986			-	693				Panereas. Prostate, Colon
495	840088			_	465			HE8QQ04	Pancreas. Prostate, Breast/Ovarian
496	840990	(AB010415) dTDP-4-keto-L-rhamnose reductase [Actinobacillus actinomycetemcomitans] >splO662511066251 DTDP-4-KETO-L-RHAMNOSE REDUCTASE. Length = 294	gnilPIDId1029073	157	1140	32	59	невам92	Panereus. Prostate
197	840992	nidogen gene product [Homo sapiens] Length = 1246	gniP1Dje218221	m	194	96	86	HE8BX38	Lung, Prostate, Colon, Breast/Ovarian
861	841009	sin3 associated polypeptide p18 [Homo sapiens] >sp 000422 000422 SIN3 ASSOCIATED POLYPEPTIDE P18. Length = 153	gip108210		523	75	75	HDTGP88	Lung, Panereas. Prostate, Colon, Breast/Ovarian

Lung. Panereas. Breast/Ovarian	Lung, Panereas, Prostate, Colon	Lung, Prostate Lung, Pancreas, Colon, Breast/Ovarian	Lung. Colon	Lung, Panereas	Prostate, Colon. Breast/Ovarian
HSKXP01	HETDILLS	HE2AY01 IINAAE75	HDQAD36	HDPDC65	HDPMF32
	74		100		96
901	ए 6		001		%
217	018	683	395	880	1244
7		402	m	656	9
gi 1373419	gi 181209		gni P1D d1019960		gi 361.55
ribosomal protein L39 [Homo sapiens] >gn PID d1012131 ribosomal protein L39 [Homo sapiens] >gi 575382 ribosomal protein L39 [Rutus norvegicus] >pir LG4229 R6RT39 ribosomal protein L39 - rat >pir G02654 (102654 ribosomal protein L39 - human Length = 51	connexin 43 [Homo sapiens] >uil29917 gap junction protein (AA 1-382) [Homo sapiens] >pir[A33853] ap junction protein Cx43, cardiac - human >splP17302 CXA1_HUMAN GAP JUNCTION ALPHA-1 PROTEIN (CONNEXIN 43) (CX43) (GAP JUNCTION 43 KD HEART PROTEIN). {		(AB000910) ribosomal protein [Sus scrofa] >gil 1684917 L44-like ribosomal protein [Homo sapiens] >gil 1666702 ribosomal protein [Mus musculus] >gi 206732 ribosomal protein L36a [Rattus norvegicus] >pir A29820 R6RT36 ribosomal protein L36a - rat Length = 106		small subunir ribonucleotide reductase [Homo sapiens] >pir[S258.46]S258.4 ribonucleoside-diphosphate reductase (EC 1.17.4.1) small chain - human Length = 389
841012	841016	841017	841032	841051	841064
499	200	501	503	504	505

Prostate. Breast/Ovarian	Lang, Prostate. Colon, Breast/Ovarian	Pancreas, Prostate	Prostate. Breast/Ovarian	Lung. Panereas. Prostate. Breast/Ovarian	Lung, Colon	Lung, Pancreus, Colon, Breust/Ovarian	Lung, Panereas. Breast/Ovarian	Lung. Panereas. Prostate. Breast/Ovarian	Pancreas. Prostate, Breast/Ovarian	Lung, Pancreas. Colon
HDPMJ48	HDPGF81	HDPKD92	HDPJR07	HDPFX64	HJMBHIS	H2LAT51	HCFLJ15	HDLAV12	HDLAB16	HDPFE82
	&		88	001		7 8	80		92	3 6
	16		%	001		8	08		54	66
608	1139	706	936	9601	1402	904	1907	256	2451	1838
- 8	162	521	_	320	1187	7	210	6	712	٣
	gi 456107		gi 57912	gi 190818		gi 32356	gni[PID d1038083		gi 186774	gi 182309
	regulatory protein [Mus musculus] >gi 452276 npdcf-1 [Mus musculus] >pir 148691 148691 regulatory protein - mouse >sp Q64322 NPD1_MOUSE NPDC-1 PROTEIN PRECURSOR. Length = 332		HCNGP gene product [Mus musculus] >pir S26660 S26660 HCNGP protein - mouse >sp Q02614 HCGP_MOUSE TRANSCRIPTIONAL REGULATOR PROTEIN HCNGP. Length = 308	quinone oxidoreductase [Homo sapiens] >gi 516534 quinone oxidoreductase2 [Homo sapiens] >pir A32667 A32667 NAD(P)H dehydrogenase (quinone) (EC 1.6.99.2) 2 - human Length = 231		L protein (AA 1-558) [Homo sapiens] >pir[A33616[A33616 heterogeneous ribonuclear particle protein L - human Length = 558	(AB013357) 49 kDa zinc finger protein [Mus musculus] Length = 460		zinc finger protein [Homo sapiens] >pir[S35305[S35305 finger protein ZNF91 - human Length = 1191	factor XIII a subunit [Homo sapiens] Length = 732
841069	841072	841078	841080	841088	841092	841095	841096	841102	841104	841108
906	507	208	809	510	511	512	513	514	\$15	516

Lung, Panereas. Prostate	Lung, Pancreas, Prostate	Prostate, Colon	Lung, Panerens. Prostate, Breast/Ovarian	Pancreas. Prostate. Breast/Ovarian	Lung. Panereus. Prostate. Colon. Breast/Ovarian	Prostate. Breast/Ovarian
Lung. Pg Prostate	Lung, Pa	Prosta	Lung. Pa Prostate, Breast/O	Pancreas. Prostate. Breast/Ov	Lung. Prosta Breast	Prostate. Breast/O
HDLAE34	HDPAE95	HDAAB17	HDAAP84	HCRMJ87	HCRNF38	HCRBS04
	001	08	66	001		
	. 00	62	¥6	001		
487	1367	358	***************************************	1040	1807	191
320	23	7	e .	39	2	324
	gniPIDje 118910	gi 1019952	gi 4063383 ·	gi 31395		
	C11 protein [Homo sapiens] >gil 1890300 eukaryotic release factor 1 [Homo sapiens] >gallPID[e118068 C11 protein [Musocricetus auratus] >pir[\$53]\$50853 translation releasing factor eRF-1 - human >spiP46055[ERF1_HUMAN EUKARYOTIC PEPTIDE CHAIN RELEASE FACT	similar to deoxyribose-phosphate aldolase [Caenorhabditis elegans] >sp Q19264 DEOC_CAEEL PUTATIVE DEOXYRIBOSE-PHOSPHATE ALDOLASE (EC 4.1.2.4) (PHOSPHODEOXYRIBOALDOLASE) (DEOXYRIBOALDOLASE). Length = 303	(AF096285) scrine-threonine kinase receptorassociated protein [Mus musculus] >sp[G4063383]G4063383 SERINE-THREONINE KINASE RECEPTOR-ASSOCIATED PROTEIN Length = 351	fibrillarin [Homo sapiens] >pir A38712 A38712 fibrillarin - human >gij3399667 (AC005393) FBRL_HUMAN; 34 KD NUCLEOLAR SCLERODERMA ANTIGEN [Homo sapiens] {SUB 4-321} Length = 321		
841118	841119	841124	841137	841143	841148	841149
517	\$ 28	519	520	521	522	523

524	841151	keratin [Carassius auratus] Length = 455	gi 212995	2	1399	4 2	2 2	HCRNY54	Lung, Panereas. Prostate, Colon. Breast/Ovarian
525	841155			103	561			HCTROF85	Prostate. BreaseOvarian
526	841161	(AB014458) ubiquitin specific protease [Homo sapiens] >sp D1035685 D1035685 UBIQUITIN SPECIFIC PROTEASE. Length = 785	gni PiD d1035685	en en	6611	\$6	95	HCL.CAS6	Lung, Prostate
527	841162	set [Homo sapiens] >pirlA57984 A45018 template activating factor-l, splice form beta - human Length = 277	gi 338039	284	1063	66		HCWFR92	Prostate, Colon
528	841163	histone H2A [Mus musculus domesticus] >pir[S45110]S45110 histone H2A - mouse >sp[Q64426]Q64426 HISTONE H2A (FRAGMENT). Length = 137	gil817939	201	665	001	001	HBMBF44	Pancreas. Breast/Ovarian
529	841169			21	440			HCFOF83	Lung, Prostate. Colon, Breast/Ovarian
530	841172	CLN3 protein [Homo supicns] >gn [P1D]e283670 CLN3 protein [Homo supicns] >gi[2947055 (AC002425) CLN3 [Homo supiens] >gi[3337387 (AC002544) CLN3 [Homo supiens] >gi[4102729 (AF015593) CLN3 protein [Homo supiens] >pir[A57219]A57219 Batten disease-related prot	gi 1039423	291	740		001	нспасвз	Prostate. Breast/Ovarian
531	841174	zinc finger protein 7 (ZFP7) [Homo sapiens] >pir A34612 A34612 zinc finger protein ZNF7 - human Length = 686	gij340446	æ	386	86	86	нсна w34	Prostate. Breast/Ovarian

241179 (AED69517) BNA hinding matein DEE-3 [Homo	Ê	101616819	4,10	577	8	0	YOU TO CALL	Luna Danieran
		101717chg	, 7	74/1	Ç.	Ç.	HCHBU80	Lung, Pancreas. Prostate
841183 keratin 18 [Homo sapiens] >gi[30708] keratin 18 precursor [Homo sapiens] >gi[34037 cytokeratin 18 [Homo sapiens] >pir[30548] keratin 18, type I, cytoskeletal - human >sp[P05783]KICR_HUMAN KERATIN, TYPE I CYTOSKELETAL 18 (CYTOKERATIN 18) (K.18) (CK.1)	_	gil386844	-	301	08		HCHCE20	Lung Panereus. Prostate, Coton. Breast/Ovarian
841186 (AJ006215) CMP-N-acetylneuraminic acid synthetase [Mus musculus] >spj088719j088719 CMP-N-ACETYLNEURAMINIC ACID SYNTHETASE (EC 2.7.7.43) (ACYLNEURAMINATE CYTIDYLYLTRANSFERASE) (CMP-SIALATE PYROPHOSPHORYLASE) (CMP-SIALATE SYNTHASE). Length = 432		gni P1D e1314953	78	1421	\$6		HCFCG26	HCFCG26 Lang, Prostate
841204 similar to beta-mannosyltransferase [Caenorhabditis elegans] >splQ22797 Q22797 SIMILAR TO BETA-MANNOSYLTRANSFERASE. Length = 487		gi 470340	-	1407	15	72	HCEF202	Lung, Panereas. Prostate, Colon
841206			251	1192			HCEEM52	Lung. Prostate
841207 (AF062484) SDP8 [Mus musculus] >sp[070493]070493 SDP8: Length = 165		gij3126981	193	585	-	63	IIMTAR23	Prostate, Colon
841211 (AC004908) zinc finger protein from gene of uncertain exon structure; similar to Q99676 (PID:g3025333) [Homo sapiens] Length = 430		gi 4159888	011	766	47	62	HCEDM42	Prostate, Breast/Ovarian

Lung, Puncreas. Prostate, Colon	Lung. Puncreus. Prostate. Breast/Ovarian	Lung, Panereas. Prostate, Colon. Breast/Ovarian	Lung, Panereas. Prostate. Breast/Ovarian	Lung, Puncreus Prostate Breast/Ovarian
нсквзог	HCEIDS#	HBMTA19	HBXFG67	HCEIC53
88	86	\$6	84	93
20	%	95	86	93
865	2298	1028	622	1199
-	_		128	m .
gi 508496	gnijPtD d1010177	gi 189246	gi 339683	gi 2198557
membrane protein [Homo sapiens] >gi 1048989 CD9 antigen [Homo sapiens] >gi 34769 MRP-1 (motility related protein) [Homo sapiens] >bbs 13135 CD9 antigen [human, teukocytes, Peptide, 228 au] [Homo sapiens] >pir A46123 A40402 CD9 antigen - human >sp P21926]	P1cdc47 [Homo sapiens] >pir[S70583]S70583 CDC47 homolog - human >sp[P33993]MCM7_HUMAN DNA REPLICATION LICENSING FACTOR MCM7 (CDC47 HOMOI.OG) (P1.1-MCM3). >gn[P1D]d1006386 hMCM2 [Homo sapiens] {SUB	NAD(P)H:menadione oxidoreduclase [Homo sapiens] >gi 189292 NAD(P)H:quinone oxireductase [Homo sapiens] >pir[A+1135 A30879 NAD(P)H dehydrogenase (quinone) (EC 1.6.99.2) 1 human >sp P1559 BHQU_HUMAN NAD(P)H DEHYDROGENASE (QUINONE) 1 (EC 1.6.99.2) (QUINON	Thy-1 [Homo sapiens] >pir A02106 TDHU Thy-1 membrane glycoprotein precursor • human Length = 161	(AD001528) spermidine aminopropyltransferase [Homo sapiens] >sp 000544 000544 SPERMIDINE AMINOPROPYLTRANSFERASE. Length = 366
841225	841229	841237	841241	841259
539	540	541	542	543

544	841260	FKBP51 [Homo sapions] >pirJC5422JC5422 FK506-binding protein, FKBP51 - human >splQ13451[FKB5_HUMAN 51 KD FK506- BINDING PROTEIN (FKBP51) (PEPTIDYL- PROLYL CIS-TRANS ISOMERASE) (EC 5.2.1.8) (PPIASE) (ROTAMASE) (54 KD PROGESTERONE RECEPTOR-ASSOCIATED IMMUNO	gil916641	m	863	∞	16	НВОРМ14	IIBODM14 Lung, Prostate
545	841264			- .	819			нвлнозз	Lung, Pancreus,
546	841275	Lutheran blood group glycoprotein [Homo sapiens] >pir[138000]138000 Lutheran blood group glycoprotein precursor - human >spip50895jLU_HUMAN LUTHERAN BLOOD GROUP GLYCOPROTEIN PRECURSOR (B- CAM CELL SURFACE GLYCOPROTEIN) (AUBERGER B ANTIGEN) (F&G253 ANTIGEN)	gi 603560	~	183	58	68	IIBGM035	Prostate. Breast/Ovarian
547	841311	(AF019661) zeta proteasome chain; PSMA5 [Mus musculus] >splG3805976[G3805976 ZETA PROTEASOME CHAIN. Length = 241	gi 3805976	45	836	001	90	HCFMY64	Lung, Pancreas. Prostate. Breast/Ovarian
248	841313	neuronal protein 15.6 [unidentified] >spl009111 009111 NEURONAL PROTEIN 15.6. Length = 133	gnt PID c274746	=	544	75	83	HBGNM82	Lung, Prostate. Colon, Breast/Ovarian
549	841317			1155	1553			HAPSG63	Lune, Prostate
250	841322	unnamed protein product [unidentified] >gil496609 basic transcripton factor 2, 44 kD subunit [Homo sapiens] >splQ13888 BASIC TRANSCRIPTION FACTOR 2, 44 KD SUBUNIT (BASIC TRANSCRIPTION FACTOR 2, 44 KD SUBUNIT (FRAGMENT), >gil1737212 basic transcription factor	gnlPIDje306259	200	1402	\$6	\$6	HAMGE23	Panéreas. Prostate

Lung. Breast/Ovarian	Lung. Prostate	Puncreas, Prostate	Lung, Panereas. Prostate, Breast/Ovarian	Lung, Panereas. Prostate. Breast/Ovarian	Prostate. Breast/Ovarian	Lung, Panereus. Colon. Breast/Oyarian
HHFJL.19	HAPQO79	HAJBU58	HAJAQ46	HMWFM73	HAJAA78	HNTCL.10
	86		94		66	£7
	86		94		96	£ .
955	3856	1363	2761	1578	562	1835
7	74	1139	61	151	7	708
ì	gi 177870		gni[PiD e218477		gi 49628	gi 178997
	alpha-2-macroglobulin precursor [Homo sapiens] >pir[A94033]MAHU alpha-2-macroglobulin precursor - human >sp[P01023]A2MG_IRUMAN ALPHA-2-MACROGLOBULIN PRECURSOR (ALPHA-2-M) >gi[825615 alpha2-macroglobulin [Homo sapiens] {SUB 672-746} Length = 1474		yeast methionyl-tRNA synthetase homolog [Homo sapiens] >pit/JC2224 JC5224 methioninetRNA ligase (EC 6.1.1.10) - human >gi 804996 mitoxantrone-resistance associated gene [Homo sapiens] {SUB 423-900} Length = 900		glucose regulated protein 94 (400 AA) [Mesocricetus auratus] >pirlA26258 A26258 endoplasmin - hamster (fragment) >spiP08712 ENPL_MESAU ENDOPLASMIN (94 KD GLUCOSE-REGULATED PROTEIN) (GRP94) (FRAGMENT). Length = 400	arginine-rich nuclear protein [Homo sapiens] >pirjA40988jA40988 54K arginine-rich nuclear protein - human >splQ05519JQ05519 ARGININE- RICH 54 KD NUCLEAR PROTEIN. Length = 484
841331	841332	841338	841345	841349	841355	841417
551	552	553	554	555	556	557

l.ung. Bread/Overian	Lung. Breast/Ovarian	Prostate, Colon	Pancreas. Prostate	Lung. Panereas. Prostate, Colon. Breast/Ovarian	Lung, Panereus, Prostate, Colon	Lung, Panereas	Lung. Breast/Ovarian	Lung. Pancreas. Prostate. Breast/Ovarian	Pancreas, Colon	Lung, Pancreas, Prostate, Breast/Ovarian
HBXDN79	HTLGV25	HI.QCP61	1111170126	HWL.1154	HHFGF52	HETJY08	HUFAB73	HYABB24	HPMSG47	HSKJF03
	901	-	7.0				92			67
	90	2 %	74				92			82
613	255	532	9 -	1612	169	836	916	1465	176	477
278	49	2 901	358	1232	7	009	20	2	780	16
	gi 3641538	pidJC5707JJC5707	gnl[PtD d1014198				gni PID e1314951			gi 3329378
	(AF073298) 4F5rel [Homo sapiens] >gi 3641536 (AF073297) 4F5rel [Mus musculus] >sp 075918 075918 4F5REL. >sp 088891 088891 4F5REL. Length = 59	HYA22 protein - human Length = 338	RTP [Homo sapiens] >gi 3046386 (AF004162) nickel-specific induction protein [Homo sapiens] >sp Q92597 Q92597 RTP, COMPLETE CDS. Length = 394				ERp28 [Homo sapiens] >spiP30040[ER29_HUMAN ENDOPLASMIC RETICULUM PROTEIN ERP29 PRECURSOR (ERP31) (ERP28). >sp[E1314951 E1314951 ERP28 PRECURSOR. Length = 261			(AF038954) vacuolar H(+)-ATPase subunii [Homo sapiens] >sp[075348 075348 VACUOLAR H(+)-ATPASE SUBUNIT. Length = 118
841548	841632	841662	841827	841835	842259	842463	842595	842722	842815	842818
858	559	5 60 5 61	562	563	264	565	999	567	268	\$69

Lung. Breast/Ovarian	Lung, Pancreus. Colon. Breast/Ovarian	Lung, Pancreas	Lung, Breast/Ovarian	Lung, Puncreus. Prostute. Breast/Ovarian	Lung, Punereas. Prostate, Colon, Breast/Ovarian	Lung, Pancreas, Breast/Ovarian	Lung. Puncreas	Lung, Panereas, Breast/Ovarian
HTL.IF83	HISCW60	HCECS78	HDPWW59	HABAE22	11E8P1356	HHEUP26	HTXOX92	HCE3165
92			100	94			78	
92			001	76			19	
745	868	1864	1966	1020	707	635	1165	244
215	563	1307	104	_	m .	378	= 3	7
gi 3766170			gi 31193	gi 3170178			gi 1825601	
(AF057297) omithine decarboxylase antizyme 2 [Homo sapiens] -gi]3766170 (AF057297) omithine decarboxylase antizyme 2 [Homo sapiens] -splG3766170[G3766170 ORNITHINE DECARBOXYLASE ANTIZYME 2gni PID d1020346 product is unknown; seizurerelated gene [Mus			Epithelin 1 & 2 [Homo sapiens] >gi 3005730 (AF055008) epithelin 1 and 2 [Homo sapiens] >pir JC1284 GYHU granulin precursor - human >sp G3005730 G3005730 EPITHELIN 1 ANI) 2. Length = 593	(AF039689) antigen NY-CO-7 [Homo sapiens] >sp O60526 O60526 ANTIGEN NY-CO-7. Length = 303			weak similarity to rat TEGT protein (GI:456207) [Caenorhubditis elegans] >sp[P91373]P91373 SIMILARITY TO RAT TEGT PROTEIN. Length = 342	
843251	843422	843784 844017	844138	844166	844194	844394	844450	844534
570	173	572 573	574	575	576	577	578	579

					•	
Lung. Breast/Ovarian	Lung, Breast/Ovarian	Lung, Puncreas. Colon	Lung. Breast/Ovarian	Colon, Breast/Ovarian	Lung. Pancreas	Lung, Panereus. Colon
HCWGE38	нррвозі	нскося	HLDDQ71	HE6BS09	HDPFV13	HCLB047
%	16	16	94		59	86
96	16	68	76		33	96
†\$ †	720	732	539	1054	1542	1013
m	-	-	. 7	7	13	99
gi 872121	gnl P1D e1254905	gi 33718	gi 179948		gi(2746788	gi 3746127
isocitrate dehydrogenase (NADP+) [Homo sapiens] >pir[S57499[S57499 isocitrate dehydrogenase (NADP+) (EC 1.1.1.42) precursor, mitochondrial - human >spiP48735[IDHP_HUMAN ISOCITRATE DEHYDROGENASE [NADP], MITOCHONDRIAL PRECURSOR (EC 1.1.1.42) (OXALOSUCCINATE	(AJ002308) synaptogyrin 2 [Homo sapiens] >sp O43760 O43760 SYNAPTOGYRIN 2. Length = 224	immunoglobulin lambda light chain gene product [Homo sapiens] >pir S25745 S25745 Ig lambda chain - human (fragment) Length = 226	cathepsin D [Homo sapiens] >gi[29678 precursor polypeptide (AA -20 to 392) [Homo sapiens] >gi[181180 preprocathepsin D [Homo sapiens] >pir[A25771[KiHUD cathepsin D (EC 3.4.23.5) precursor - human >sp[P07339]CATD_HUMAN CATHEPSIN D PRECURSOR (EC 3.4.23.5).		(AF040642) contains similarity to transacylases [Caenorhabditis elegans] >sp 044793 044793 C50D2.7 PROTEIN. Length = 895	E25B protein [Mus musculus] >spl089051 089051 E25B PROTEIN. Length = 266
844535	844644	844653	844659	844796	844812	844894
280	185	582	283 ·	584	585	586

		·				
HHEUJ91 Panereas, Colon	Lung, Panereas, Prostate, Breast/Oyarian	Lung, Pancreas. Colon. Breast/Ovarian	Lung, Pancreas. Prostate. Breast/Ovarian	Lung. Brand Morrison	Panerens, Colon.	Pancreas. Breast/Ovarian
НИЕОЛЯ	HWHGQ46	HCFNA68	НКЛЈW79	HKDAF83	HSODT09	HADAB09
001		06	6			
20		06	16			
1232	. 1254	2	1365	261	509	1677
39	208		-	-	180	1369
gi 387020		gil3 12407	gil2130527			
phosphoglycerate kinase (EC 2.7.2.3) [Homo sapiens] >gi]387021 phosphoglycerate kinase [Homo sapiens] >gi[35435 coding sequence [Homo sapiens] >pir[159050]KIHUG phosphoglycerate kinase (FC 2.7.2.3) - human Length = 417		leukocyte antigen F [Homo sapiens] >gi 3273731 (AF055066) MHC class I HLA-F [Homo sapiens] >pir A60384 A60384 MHC class I histocompatibility antigen HLA-F alpha chain Dew3 precursor - human >spl P30511 HLAF_HUMAN HLA CLASS I HISTOCOMPATIBILITY ANTIGEN, F A	Cyr61 [Homo sapiens] >gnl[PID]e311857 Gig1 protein [Homo sapiens] >gi[2196782 (AF003594) growth-factor inducible immediate early gene product CYR61 [Homo sapiens] >gnl[PID]e1249319 hCYR61 protein [Homo sapiens] >spl[O00622]CYR6_HUMAN CYR61 PROTEIN PRECURSO			
845361	845620	845639	845660	845720	845785	X45897
587	288	286	. 80	165	292	593

				·		
Lung. Panereas. Colon	Lung, Pancreas	Lung, Pancreas, Prostate, Colon. Breast/Ovarian	Lung, Panereas	Lung. Prostate Lung.	Breast/Ovarian	Lung, Pancreas, Colon. Breast/Ovarian
HWI.QQ65	HDPIT90	HLJCQ57	нсмржог	HPWDE09 HTXPN06	1101 4012	HWAFUI6
00	97	88			ē,	. %
001	97	84	16		7	: %
1239	337.	585	1051	651 286	15	320
-	47	127	53	286		. m
gi 2182269	gnl PID d1032501	gi 203072	gi 38318			gn PtD d1019961
beta actin [Ovis aries] >gi 2661136 (AF035774) beta actin [Equus caballus] >gi 3320892 (AF076190) beta-actin [Trichosurus vulpecula] >gi 177968 cytoplasmic beta actin [Homo sapiens] >gn PID u1021082 (AB004047) beta-actin [Homo sapiens] >gi 28252 beta-act	(AB005894) ecalectin [Homo sapiens]. >sp 075028 075028 ECALECTIN. Length = 323	0-44 protein [Rattus sp.] >pir 157612 157612 Rat brain 0-44 mRNA, segment 2 - rat >sp P38718 P044_RAT 0-44 PROTEIN. Length = 127	protein p68 (AA 1-614) [Homo sapiens] >gij35220 p68 protein (AA 1-614) [Homo sapiens] >gij2599360 (AF015812) RNA helicase p68 [Homo sapiens] >pirJC1087JJC1087 RNA helicase, ATP- dependent - human >splP17844[DDX5_HUMAN PROBABLE RNA-DEPENDENT HELICASE P68		·	HWAFU16R (AB000911) ribosomal protein [Sus scrofa] >gnllP1Dje1339008 (AL031228) dJ1033B10.4 (40S ribosomal protein S18 (RPS18, KE-3)) [Homo sapiens] >gi 198380 ribosomal protein [Mus musculus] >gi 433447 ribosomal protein S18 [Rattus rattus] >gi 3811382 (AF100956)
845922	846016	846040	846073	846257 HTXPN06R	1121,A012R	HWAFUIGR
594	595	296	597	598 599	009	109

Pancreas. Colon. Breast/Ovarian	Lung, Colon. Breast/Ovarian	Lung, Colon	Lung, Colun, Breast/Ovarian	Lung, Panereas. Colon	Colon. Breast/Ovarian	Lung. Colon
НАЕАМ91	HOEMT44	HE2OW04	HECF025	HAPQP94	112CB137	НЕОРОІЗ
99	93	68	87	7.6	7 9	83
99	84	83	6.5	76	3	80
215	431	297	11 3	320	18.7	216
174	\$4	,	m	m	m	83
gni P1D d1026481	gni P1D d1033048	gi 2581793	gi[2307014	gi 2443581	gi 2792508	gi 3372377
HAEAM91R (AB005218) L subunit of photosynthetic reaction center complex [Acidiphilium rubrum] >gnl[PID]d1026488 (AB005219) L subunit of photosynthetic reaction center complex [Acidiphilium angustum] >spl(070105(0701051. SUBUNIT OF PHOTOSYNTHETIC REACTION CENTER COM	HOEMT44R (AB010959) natural killer cell enhancing factor [Cyprinus carpio] Length = 199	(AF001631) glucose-regulated protein GRP94 [Oryctolagus cuniculus] >splO18750jENPL_RABIT ENDOPLASMIN (94 KD GLUCOSE-REGULATED PROTEIN) (GRP94) (FRAGMENT). Length = 716	(AF012422) ribosonnal protein 46 [Drosophila inclanogaster] Length = 51		(AF042107) ribosomal protein S3a [Eimeria tenella] >gi 2792508 (AF042107) ribosomal protein S3a [Eimeria tenella] Length = 264	HEOPQ13R (AF042505) cytochrome b [Homo sapiens]
HAEAM9IR	HOEMT44R	HE2OW04R	HPCPG25R	HAPQP94R	H2CBI37R	неороізк
602	603	604	\$09	909	607	809

609	HCRNC25R	HCRNC25R (AF051894) 15 kDa selenoprotein [Homo sapiens] Length = 161	gi 3095111	19	162	901	100	HCRNC25	Lung, Panereas, Colon
610	III:ITF28R	(AF056218) superficial zone protein [Box taurus] >spi077765[O77765 SUPERFICIAL ZONE PROTEIN (FRAGMENT). Length = 401	gi 3676501	~	185	23	08	HF17F28	Punerens, Colon
611	H2LAY26R			24	155			H2LAY26	Panereas, Colon
612	HAPQA06R	HAPQA06R 40-kDa keratin protein [Homo sapiens] >pir A31370 KRHU9 keratin 19, type 1, cytoskeletal - human Length = 400	gij386803	7	355	62	62	HAPQA06	Lung, Pancreas. Colon, Breast/Ovarian
613	HAQBM72R	HAQBM72R 40-kDa keratin protein [Homo sapiens] >pirjA31370 KRHU9 keratin 19, type 1, cytoskeletal - human Length = 400	gi 386803	61	145		≂	HAQBM72	Pancreas, Colon
614	HBGOK 18R	HBGOK 18R 40-kDa keratin protein [Homo sapiens] - pirjA31370[KRHU9 keratin 19, type 1, cytoskeletul - human Length = 400	gi 386803	_	429	16	93	HBGOK18	Lung, Pancreas. Colon, Breast/Ovarian
615	H2MAC07R	H2MAC07R acidic ribosomal phosphoprotein (P1) [Homo sapiens] > pirlB27125[R6HUP1 acidic ribosomal protein P1 - human Length = 114	gi 190234	Ξ	458	001	001	H2MAC07	Lung. Colon. Breast/Ovarian
919	HT WKF26R	HTWKF26R acidic ribosomal phosphoprotein (P2) [Homo sapiens] > pirJC27125[R6HUP2 acidic ribosomal protein P2 - human Length = 115	Bil 190236	-	345	95	96	HTWKF26	Lung, Panereas. Breast/Ovarian
617	HTAHR89R	HTAHR89R ADP,ATP carrier protein T2 - human >splP12236/ADT3_HUMAN ADP,ATP CARRIER PROTEIN, LIVER ISOFORM T2 (ADP/ATP TRANSLOCATOR 3) (ADENINE NUCLEOTIDE TRANSLOCATOR 3) (ADT 3) Lenoth = 298	pir S03894 S03894	13	408	96	%	HTAHR89	Lung, Pancreas

HOACE24 Panereas, Colon	Lung, Panerens. Breast/Ovarian	Lung. Panereas. Colon. Breast/Ovarian	Lung, Colon. Breast/Ovarian	Lung, Panereas
HOACE24	НОЕГ.С27	HWI.BS25	HWLVW62	HALSE08
8	001	93	16	76
16	001	06	24	26
374	604	95	213	233
m	89	m	-	m
gil178372	មរុ178351	gi 409191	gi 180414	spP01011AACT_H UMAN
HOACE24R alcohol dehydrogenase [Homo sapiens] >pir[A33371 DEHUE1 aldehyde dehydrogenase (NAD+) (EC 1.2.1.3) 1. cytosolic - human >sp P00352 DHAC_HUMAN ALDEHYDE DEHYDROGENASE, CYTOSOLIC (EC 1.2.1.3) (CLASS I) (ALHDII) (ALDH-EI). (SUB 2-501) Length = 501	aldolase A (EC 4.1.3.13) [Homo sapiens] >gi[28597] aldolase A (AA 1-364) [Homo sapiens] >pir[314084]ADHUA fructose-bisphosphate aldolase (EC 4.1.2.13) A - human >spiP04075]ALFA_HUMAN FRUCTOSE- BISPHOSPHATE ALDOLASE A (EC 4.1.2.13) (MUSCLE-TYPE ALDOLASE). (S	HWLBS25R aldolase A [Gallus gallus] >gil409193 aldolase A [Gallus gallus] >bbs 167536 aldolase C=fructose-1,6-biphosphate aldolase {EC 4.1.2.13} {chickens, brain, Peptide Partial, 42 aa] {Gallus gallus} >pit 15129 15129 aldolase C - chicken (fragment) Length = 4	HWLVW62R alpha-I type III collagen [Homo sapiens] Length = 345	HALSE08R ALPHA-I-ANTICHYMOTRYPSIN PRECURSOR sp P01011 AACT_H (ACT). >gi 4165890 (AF089747) alpha-1- antichymotrypsin precursor [Homo sapiens] {SUB 17-423} >gi 177933 alpha-1-antichymotrypsin precursor [Homo sapiens] {SUB 22-423} >gi 28332 alpha 1 antichymotrypsin [Homo sapiens] {SU
H0ACE241	HOELC27R	HWLBS25F	HWLVW628	HALSE08R
819	619	620	621	622

Pancreas, Breast/Ovarian	Lung, Colon. Breast/Ovarian	Pancreas, Colon, Breast/Ovarian	Panereas, Colon	Lung, Puncreas, Colon	Pancreas. Colon Pancreas. Colon Pancreas. Colon
HFKHD94	НСЕ2М86	HOF OA 89	HBWCN69	HLQGB43	HCROL58 HS2IF12 HWLWA01
. 6	08	P6	06	001	
76	\$5	7 6 .	&	001	
316	165	399	308	78	506 475 538
7	8	154	09		3 83 2
gi 30076	gil49878	gi 178699	gi 902745	gil 79318	
alpha-2 chain precursor (AA -25 to 1018) (3416 is 2nd base in codon) [Homo sapiens] Length = 1043	alpha-adaptin (A) (AA 1-977) [Mus musculus] >pir[A3011][A3011] alpha-adaptin A - mouse >spl 17426[ADAA_MOUSE ALPHA-ADAPTIN A (CLATHRIN ASSEMBLY PROTEIN COMPLEX 2 ALPHA-A LARGE CHAIN) (100 KD COATED VESICLE PROTEIN A) (PLASMA MEMBRANE ADAPTOR HA2/AP2 ADAPT	annexin IV (placental anticoagulant protein II) [Homo sapiens] >gul[PID]d1011889 annexin IV (carbohydrtate-binding protein p33/41) [Homo sapiens] >pir[A42077]A42077 annexin IV - human >splP09525[ANX4_HUMAN ANNEXIN IV (LIPOCORTIN IV) (ENDONEXIN I) (CHROMOB	HB WCN69R beta-1,2-N-acetylglucosaminyltransferase II [Homo sapiens] >pir S66256 S66256 alpha-1,6-mannosylglycoprotein beta-1, 2-N-acetylglucosaminyltransferase (EC 2.4.1.143) - human >sp Q10469 GNTZ_HUMAN ALPHA-1,6-MANNOSYL-GLYCOPROTEIN BETA-1,2-N-ACETYLGLUCOSAM	HI.QGB43R beta-2-microglobulin [Homo sapiens] Length = 119	
HFKHD94R	НСЕ2М86 R	HOFOA89R	HBWCN69R	HLQGB43R	HCROL58R HS2IF12R HWLWA01R
623	624	625	929	627	628 629 630

631	HCHMV24R			12	185			HCHMV24	Pancreas, Colon.	
632	HCHPT49R			94	303			HCHPT49	Colon. Breast/Ovarian	
633	HCRMG12R			۲۱	187			HCRMG12	Pancreas, Colon	
634	HWLWE68R			2	241			HWLWE68	Pancreas, Colon	
635	HCHPF59R			24	113			HCHPF59	Pancreas. Breast/Ovarian	
989	HS21A81R			8	551			HS21A81	Pancreas, Colon	
637	HCRNC17R			Ξ	400			HCRNC17	Pancreas, Colon	
638	HISDJ39R			14	406			HISD139	Pancreas, Colon	
639	HWLEL43R			7	337			HWLEL43	Pancreas, Colon	
640	HASCG71R			16	249			HASCG71	Lung, Colon, Breast/Ovarian	
641	HOEMO43R			7	184			НОЕМО43	Lung. Panereas. Colon. Breast/Ovarian	
642	HRDFT95R	c-erb-B-2 precursor [Homo sapiens] >pir A24571 A2457 protein-tyrosine kinase (EC 2.7.1.112) erbB2 precursor - human >sp P04626 ERB2 HUMAN ERBB-2 RECEPTOR PROTEIN-TYROSINE KINASE PRECURSOR (EC 2.7.1.112) (P185ERBB2) (NEU PROTO- ONCOGENE) (C-ERBB-2) Length	gi(31198		23.1	76	83	HRDF795	Panereas, Colon	
643	HAGEP27R	HAGEP27R C10 protein [Bos taurus] >pir A38464 A38464 33K laminin receptor homolog - bovine Length = 295	gi 163303	m	137	98	98	HAGEP27	Lung, Pancreas. Colon. Recost/Overtim	

Colon	HI, IDZ 15 Lung, Colon	Lung, Panereas	Lung, Pancreas
HSYDG18	HLJDZ15	IIAIIDQ54	HTLHII8
<u>.</u>	7.	001	88
001	. 12	001	88
422	011	103	48 1
m	m	7	7
Bil825635	gi 1006657	gil 179948	pir S05378 CGHU2A
calmodulin [Homo sapiens] >splQ13942[Q13942 CALMODULIN. >pirJA56785[A56785 calmodulin - pig (fragment) {SUB 80-130} >gi[324322 (AF069912) calmodulin {Xiphias gladius} {SUB 80-114} >pir[E44101[E44101 calmodulin. vasoactive intestinal peptide-binding prote	cathepsin C [Homo sapiens] > gil 1947071 prepro dipeptidyl peptidase I [Homo sapiens] > pirl 566504 S66504 dipeptidyl-peptidase I (EC 3.4.14.1) precursor - human > spip 153634 CATC_HUMAN DIPEPTIDYL-PEPTIDASE I PRECURSOR (EC 3.4.14.1) (DPP-1) (CATHEPSIN C) (CATHE	HAHDQ\$4R cathepsin D [Homo sapiens] >gi[29678 precursor polypeptide (AA -20 to 392) [Homo sapiens] >gi[181180 preprocathepsin D [Homo sapiens] >pir[A2577 [KHHUD cathepsin D (EC 3.4.23.5) precursor - human >sp P07339 CATD_HUMAN CATHEPSIN D PRECURSOR (EC 3.4.23.5).	collagen alpha 2(VI) chain precursor, long splice form - human >gi[179711 alpha-2 collagen type VI-a' [Homo sapiens] {SUB 590-1018} >gi[291918 alpha-2 type VI collagen [Homo sapiens] {SUB 315-338} Length = 1018
HSYDG18R	HLJDZ1SR	HAHDQ54R	HTCHI18R
444	645	646	647

Lung, Pancreus, Breust/Ovarian	Lang, Panerens. Colon, Breast/Ovarian	Pancreas. Breast/Ovarian	Pancreas. Colon, Breast/Ovarian	Lung, Pancreas, Colon
HACAC47	III.QI:Y41	HOFMO83	HFTDR22	HPICZ01
08	*	93	001	95
62	9 6		001	4
315	377	205	357	163
 -	m	7	136	7
gi 179665	gi 179665	gnijP1Djd1012016	pir S07959 S07959	gi 342255
HACAC47R complement component C3 [Homo sapiens] >pirJA94065 C3HU complement C3 precursor- human >spiP01024 CO3 HUMAN COMPLEMENT C3 PRECURSOR [CONTAINS: C3A ANAPHYLATOXIN] >gil181130 complement component C3 [Homo sapiens] {SUB 1-24} Length = 1663	III.QFY41R complement component C3 [Humo sapiens] >pirJA94065[C3HU complement C3 precursor- human >sp P01024 CO3 HUMAN COMPLEMENT C3 PRECURSOR [CONTAINS: C3A ANAPHYLATOXIN]. >gi 181130 complement component C3 [Homo sapiens] {SUB 1-24} Length = 1663	HOFMO83R cyclin G [Homo sapiens] >gi 1236233 cyclin G1 [Homo sapiens] >gi 1236913 cyclin G1 [Homo sapiens] >pir G02401 G02401 cyclin G1 - human >spiens] >pir G02401 G02401 cyclin G1 - human >spiPs1959 CG2G_HUMAN G2/MITOTIC- SPECIFIC CYCLIN G1. >gn PID d1013694 cyclin G [Homo sapiens] {SUB 1-279} >gi 1486361 c	HFTDR22R cytochrome b5, hepatic - brown howler monkey (fragment) Length = 87	
HACAC4	III.QFY4	ноғмо8	HFTDR22	HPJCZOIR
648	649	650	651	652

Lung, Pancreas, Colon	Lung. Pancreas. Colon	Lung, Pancreus. Colon	Lung, Pancreas	Panereus, Colon
HOEKC39	HOEL124	HODEI18	HOSNR06	нсорг20
56	.26	22	\$6	86
16	76	69	, £	86
167	991	180	403	245
4.	29	-	569	36
Bil13006	gi 2052365	gi 530069	gil530069	gi 181346
IIOEKC39R cytochrome oxidase 1 [Homo sapiens] >gi[506829 cytochrome oxidase subunit 1 [Homo sapiens] >pir[A00463]ODHU1 cytochrome-c oxidase [EC 1-9.3.1) chain 1 - human mitochondrion (SGC1) >splP00395 COX1_HUMAN_CYTOCHROME_C OXIDASE_POLYPEPTIDE 1 (EC 1.9.3.1). Leng	HOELI24R cytochrome oxidase subunit 3 [Homo sapiens] Length = 260	cytochrome oxidase subunit II [Homo sapiens] >gi[530071 cytochrome oxidase subunit II [Homo sapiens] >gi[530073 cytochrome oxidase subunit II [Homo sapiens] >gi[530077 cytochrome oxidase subunit II [Homo sapiens] >gi[337187 cytochrome oxidase subunit II [Homo sapiens] >gi[337187 cytochrome oxidase subunit II [HOSNR06R cytochrome oxidase subunit II [Homo sapiens] >gi 530071 cytochrome oxidase subunit II [Homo sapiens] >gi 530073 cytochrome oxidase subunit II [Homo sapiens] >gi 530077 cytochrome oxidase subunit II [Homo sapiens] >gi 53077 cytochrome oxidase subunit II [Homo sapiens] >gi 337187 cytochrome oxidase	HCQDL20R cytochrome P450 PCN3 [Homo sapiens] -pir[A34101[A34101 cytochrome P450 3A5-human -sp[P20815]CP35_HUMAN CYTOCHROME P450 3A5 (EC 1.14.14.1) (CYPI11A5) (P450-PCN3). >gil950342 cytochrome P450 [Homo sapiens] {SUB 1-24} Length = 502
HOEKC39R	HOELI24R	HODE118R	HOSNROGR	HCQDL20R
. 653	654	655	656	657

Lung. Breast/Ovarian	Pancreus. Colon	Pancreas, Colon	Lung, Punerens, Colon	Lung. Panereas, Colon. Breast/Ovarian	Panereas, Colon
HCFLM34	HTTID16	HDPA145	HKIXL19	H2LAY52	HAJRBO9
%	88	65	001	001	77
94	8	\$9	001	001	12
308	331	181	348	494	324
& 4 &	7	2	-	27	61
gi 553907	gi 684922	gi 402207	gi 450271	gi 488513	gi 1006659
elongation factor Tu [Mus musculus] >sp[Q61311[Q61311 EUKARYOTIC TRANSLATION ELONGATION FACTOR I ALPHA I (EEF-TU GENE ENCODING EI.ONGATION FACTOR TU, S' END) (FRAGMENT). Length = 108	ENA-78 prepeptide [Homo sapiens] >gi]607031 neutrophil-activating peptide 78 [Homo sapiens] >gi[471243 ENA-78 gene product [Homo sapiens] >pit]C2433[A55010 neutrophil-activating peptide ENA-78 - human >spi[P42830]EN78_HUMAN NEUTROPHIL ACTIVATING PROTEIN E	endoglin [Homo sapiens] >pir S37628 S37628 endoglin - human Length == 625	epoxide hydrolase [Homo sapiens] >gij340390 epoxide hydrolase [Homo sapiens] >gij34543 epoxide hydrolase (AA 1-455) [Homo sapiens] >gij458701 epoxide hydrolase [Homo sapiens] >pirjA29939 A29939 epoxide hydrolase (EC 3.3.2.3) 1, microsomal - human >spll9070	EWS gene product [Mus musculus] >pir A53726/A55726 RNA-binding protein Ews - mouse >sp Q61545 EWS_MOUSE RNA-BINDING PROTEIN EWS. Length = 655	FAST kinase (Homo sapiens) >pirl137386 137386 FAST kinase - human >splQ14296 Q14296 FAST KINASE. Length = 549
HCFLM34R	H1TID16R	HDPA145R	HKIXL19R	H2LAY52R	HAJRB09R
665	999	299	899	699	670

Lung. Colon	Pancreas, Colon	Lung, Panereas, Prostate, Colon, Breast/Ovarian	Panereas, Colon. Breast/Ovarian	Colon. Breast/Ovarian
HAPN186	HCEVB92	HAPRJ22	HCRMZ32	IIBMVM42
97	≅	100	- 16	. 87
76	78	.00	- 6	25
419	217	-64	316	363
m	7	168	7	_
gi 287865	gi 183056	gi 31831	gi 183082	gi 484102
HAPNI86R G9a [Homo sapiens] >pir\S30385\S30385\G9a protein - human >sp Q14349 Q14349\G9A PROTEIN CONTAINING ANKYRIN-LIKE REPEATS. Length = 1001	HCEVB92R glutamate dehydrogenase [Homo sapiens] >spjQ14400jQ14400 GLUTAMATE DEHYDROGENASE (FRAGMENT). Length = 258	glutamateammonia ligase [Homo sapiens] >pir[S18455[AJHUQ glutamateammonia ligase (EC 6.3.1.2) - human Length = 373	HCRMZ32R glutamine:fructose-6-phosphate amidotransferase [Homo sapiens] >pirJA45055[A45055 glutamine-fructose-6-phosphate transaminase (isomerizing) (EC 2.6.1.16) - human >splQ06210[GFAT_HUMAN GLUCOSAMINE-FRUCTOSE-6-PHOSPHATE AMINOTRANSFERASE [ISOMERIZING] (EC 2	HIBMVM42R guanine nucleotide regulatory protein [Homo sapiens] >gij304 1860 (AC004534) guanine nucleotide regulatory protein [Homo sapiens] >pir[138402]138402 guanine nucleotide regulatory protein - human >spiQ12774(Q12774 GUANINE NITCLEOTIDE REGILI ATTORY PROTEIN Lene
HAPNI86R	HCEVB92R	HAPRJ22R	HCRMZ32R	HI3MVM42R
129	672	673	674	675

Lang, Panereas. Colon	Lung, Panereas, Colon	Coton. Breast/Ovarian	Lung. Colon	Lung, Colon	Lung, Pancreus, Colon	Lung. Pancreus. Colon	Panerans, Colon
HADCH:45	HTXPNII	HCDBN37	HABGC02	HNTSA70	HDTKP24	HODEI14	HOELC42
96	80 60	96	8	72	29	89	
96 .	46	96	68	69	\$	62	26
439	413	300	389	341	492	247	
6	m	-	e	m	397	164	ដ
gi 386746	gi 188492	pirjA44192JA44192	gi 490048	gni[P1D d1013380	pirJC1348JC1348	piqJC1348 JC1348	gi 184816
guanine nucleotide-binding protein G-s-alpha-4 [Homo supiens] >gi[31913 alpha-St (AA 1-380) [Homo sapiens] >pin[C31927]RGHUA1 GTP-binding regulatory protein Gs alpha chain (adenylate cyclass-stimulating). splice form 4 - human Length = 380	heat shock-induced protein [Homo sapicns] >pir B45871 B45871 dnaK-type molecular chaperone HSP70-Hom - human >sp P34931 HS7H_HUMAN HEAT SHOCK 70 KD PROTEIN 1-HOM (HSP70-HOM). Length =	heterogeneous nuclear ribonucleoprotein C-like protein - human Length = 328	HABGC02R HLA-DR-beta-B [Homo sapiens] Length = 266	HsMcm6 [Homo sapiens] >splQ14566[MCM6_HUMAN DNA RIPLICATION LICENSING FACTOR MCM6 (P105MCM). Length = 821	hypothetical 18K protein (rRNA) - goldfish milochondrion (SGC1) Length = 166	hypothetical 18K protein (rRNA) - goldIish mitochondrion (SGC1) Length = 166	IGF-BP 4 [Homo sapiens] >gn PID e1227579 insulin-like growth factor binding protein 4 [Homo sapiens] >pir B37252 B37252 insulin-like growth factor-binding protein 4 precursor - human >sp P22692 IBP4_HUMAN INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 4 PREC
HADGE45R	HTXPNIIR	HCDBN37R	HABGC02R	HNTSA70R	HIJTKP24R	HODE114R	HOELC42R
929	677	829	629	089	189	682	683

684	HWAFL44R	HWAFL44R immunoglobulin heavy chain [Homo sapiens] >pirlD36005 D36005 Ig heavy chain V region (M43) - human {SUB 38-156} Length = 156	gi 567121	7	463	83	06	HWAFL44	Lung, Colon
985	HABGF46R	HABGF46R immunoglobulin light chain variable region Homo sapiens] > gi 2970534 (AF049692) immunoglobulin kappa light chain [Homo sapiens] {SUB 3-106} Length = 143	gi 1136555	42	446	12	\$	IIABGF46	Lung, Panereas. Colon, Breast/Ovarian
989	HOELC15R	insulin-like growth factor-binding protein [Homo sapiens] >gi[38679] growth factor-binding protein-3 [Homo sapiens] >gi[398164 insulin-like growth factor binding protein 3 [Homo sapiens] >pir[A36578 OHU3 insulin-like growth factor-binding protein 3 precu	gi 183116	∞	424	96	96	HOEI.C15	Pancreus, Colon. Breust/Ovarian
687	H2LAR26R	keratin 18 [Homo sapiens] >gi 307081 keratin 18 precursor [Homo sapiens] >gi 34037 cytokeratin 18 [Homo sapiens] >pir S05481 S05481 keratin 18, type I, cytoskeletal - human >sp P05783 K1CR_HUMAN KERATIN, TYPE 1 CYTOSKELETAL 18 (CYTOKERATIN 18) (K18) (CK 1	gi 386844	5.	476	76	86	H2LAR26	Colon. Breast/Ovarian
889	H2LAV85R	Ku (p70/p80) subunit [Homo sapiens] >gi]307093 Ku antigen [Homo sapiens] >pirla3505 la32626 Ku antigen 80K chain - human >sp[p13010]KU86_HUMAN ATP-DEPENDENT DNA HELICASE II, 86 KD SUBUNIT (LUPUS KU AUTOANTIGEN PROTEIN P86) (86 KD SUBUNIT OF KU ANTIGEN) (T	gi]307094		462	76	86	H2LAV85	Lung. Panereas
689	HBSDC92R	HBSDC92R I-caldesmon II [Homo sapiens] Length = 532	gnliPID d1015132	95	337	99	97	HBSDC92	Lung. Breast/Ovarian

		•					
Lung, Pancreas. Colon. Breast/Ovarian	Lung, Panereas	Pancreas, Breast/Ovarian	Pancreas. Colon	Pancreas, . Breast/Ovarian	Pancreas, Colon	Lung. Colon	Lung. Panerens
HUTHNOT	H2L.A.W03	ПОЕМОЮ	HKAH114	НОНЕА39	HOELF72	HAPNX59	HBJJS17
5	002	\$\$		86	76	88	001
16	66			88	. 97	88	001
545	536	201	216	240	468	432	255
87	Ξ		_	_	28		-
gi 186804	gni[PID c223241	gi 780261		pirjA55494 A55494	gi 699577	gi 312142	gi 903982
L6 [Homo supiens] >pir A42926 A42926 L6 surface protein - human Length = 202	H2LAW03R lactate dehydrogenase B [Homo sapiens] >gi[34329] lactate dehydrogenase B (AA 1 - 334) [Homo sapiens] >pir[802795]DEHULH L-lactate dehydrogenase (EC 1.1.1.27) chain H · human >sp P07195 LDHH HUMAN L-LACTATE DEHYDROGENASE H CHAIN (EC 1.1.1.27) (LDI1-B). (SUB	H()I:MO60R lactate dehydrogenase-A [Homo sapiens] >gi[34313] lactate dehydrogenase-A [Homo sapiens] >pir[A00347]DEHULM L-lactate dehydrogenase (EC 1.1.1.27) chain M - human >spiP00338]LDHM_HUMAN L-LACTATE DEHYDROGENASE M CHAIN (EC 1.1.1.27) (LDH-A). (SUB 2-332) Lengt		latent transforming growth factor-beta-binding protein - human Length = 1820	lumican [Homo sapiens] Length = 338	M130 antigen [Homo sapiens] >pir 138003 S36077 M130 antigen - human >splQ07898 Q07898 M130 ANTIGEN PRECURSOR. Length = 1116	methionine aminopeptidase [Homo sapiens] -gil687243 eIF-2-associated p67 homolog [Homo sapiens] -pirJS52112[DPHUM2 methionyl aminopeptidase (EC 3.4.11.18) 2 - human -splp50579[AMP2_HUMAN METHIONINE AMINOPEPTIDASE 2 (EC 3.4.11.18) (METAP 2) (PEPTIDASE M 2)
HUTHNOIR	H2LAW03R	HOI:MO60R	HKAHJ14R	нонеаз98	HOELF72R	HAPNX59R	HBJJS17R

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HATDU61 Panereas, Colon	Prostate, Colon	Pancreas, Colon	Colon, Breust/Ovarian
HATDUĞ	HCWHT65	H2CBN02	H2CBV68
C 9		66	001
63	74	66	001
801	432	435	406
- : :	-	-	8
gil182651	gi 1763642	gil190127	gil190127
HATDU61R midkine [Homo sapiens] >gi 188571 retinoic acid inducible factor [Homo sapiens] >gi 35087 neurice outgrowth-promoting protein [Homo sapiens] >gn [PtD]dt1001932 midkine [Homo sapiens] >pirJ110385J110385 midkine precursor - human >sp P21741 MK_HUMAN MIDKINE	5R mitochondrial intermediate peptidase precursor [Homo sapiens] >spl099797 Q99797 MITOCHONDRIAL INTERMEDIATE PEPTIDASE PRECURSOR (EC 3.4.24.59). Length = 713	Amitochondrial matrix protein [Homo sapiens] -pir[A32800]A32800 chaperonin GroEL precursor- human -spip 10809]P60_HUMAN MITOCHONDRIAL MATRIX PROTEIN PI PRECURSOR (P60 LYMPHOCYTE PROTEIN) (60 KD CHAPERONIN) (HEAT SHOCK PROTEIN 60) (HSP-60) (PROTEIN CPN60) (R mitochondrial matrix protein [Homo sapiens] -pirjA32800JA32800 chaperonin GroEL precursor- human -splP10809JP60_HUMAN MITOCHONDRIAL MĀTRIX PROTEIN P1 PRECURSOR (P60 LYMPHOCYTE PROTEIN) (60 KD CHAPERONIN) (HEAT SHOCK PROTEIN 60) (HSP-60) (PROTEIN CPN60) (
HATDU61	HCWHT65R	H2CBN02R	H2CBV68R
869	669	700	102

Lung. Breast/Ovarian	Lung, Pancreas. Colon	Lung, Colon. Breast/Ovarian	Pancreas, Colon	Lung, Pancreas	Lung, Pancreas. Colon, Breast/Ovarian
H6EDK07	НАСАНІО	HCCMC56	H2CBN54	HMCGLI2	HWHPX50
06	96	88	66	28	8
06	68	83	66	76	87
252	99	351	427	389	4 -
- .	_	91		96	_
gni P1D d1011683	bbs 75898	SPI 17568INB8M_H UMAN	bbs 178894	gi 666043	gi 200011
Mr 110,000 antigen [Homo sapiens] >pir 152703 152703 42K membrane glycuprotein - human >sp Q16186 G100_HUMAN 110 KD CELL MEMBRANE GLYCOPROTEIN. Length = 407	NADH dehydrogenase subunit 2, ND2 [human, brain, Peptide Mitochondrial Partial Mutant, 67 au] [Homo sapiens] >splQ36734 Q36734 NADH DEHYDROGENASE SUBUNIT 2 (FRAGMENT). Length = 67	HCCMC56R NADH-UBIQUINONE OXIDOREDUCTASE B18 spP17568 NB8M_H SUBUNIT (EC 1.6.5.3) (EC 1.6.99.3) (COMPLEX UMAN I-B18) (CI-B18) (CELL ADHESION PROTEIN SQM1). Length = 134	NADH-ubiquinone oxidoreductase B22 subunit {C-terminal} {human, placenta, Peptide Mitochondrial Partial, 179 aa] {Homo sapiens Length = 179	HMCGL12R NMB gene product [Homo sapiens] >pir[138065[138065 gene NMB protein - human >sp[Q14956]NMB_HUMAN PUTATIVE TRANSMEMBRANE PROTEIN NMB PRECURSOR. Length = 560	HWHPX50R nuckolar protein [Mus musculus] >pir[152858 152858 nuckolar protein - mouse >spl061937 NPPM_MOUSE NUCLEOPHOSMIN (NPM) (NUCLEOLAR PHOSPHOPROTEIN B23) (NUMATRIN) (NUCLEOLAR PROTEIN NO38). Length = 292
H6EDK07R	HACAH10R	HCCMC56R	H2CBN54R	HMCGLI2R	HWHPX50R
702	703	704	705	706	707

708	HAPQD84R			115	267			HAPQD84	Lung, Pancreas. Colon
709	HL.IBN66R		-	_	916			SANGL	Breast/Ovarian
710	HE2BD84R	OSF-2p1 [Homo sapiens] > pirfS3611t S36111 osteoblast-specific factor 2 - human >sp Q15064 Q15064 OSF-2P1. Length = 779	gn P1D d1003341	. 2	394	1.		HE2BD84	Pancreas, Colon. Breast/Ovarian
117	HI.QFY45R	HI.QFY45R pancreatitis-associated protein [Homo sapiens] >bgi]312807 preprotein [Homo sapiens] >bbs 121222 PAP-H=pancreatitis-associated protein [human, pancreas, Peptide, 175 aa] [Homo sapiens] >gn PID d1003233 PAP homologous protein [Homo sapiens] >pir A49616 A49	gi 482909	75	374	99	99	111.QFY45	Panereas, Colon
712	HAMGQ78R	HAMGQ78R phosphate carrier isoform A (alternatively spliced, exon IIIA) - human >splQ00325IMPCP_HUMAN MITOCHONDRIAL PHOSPHATE CARRIER PROTEIN PRECURSOR. Length = 362	pidA53737 A53737	2	352	83	83	HAMGQ78	HAMGQ78 Lung. Colon
713	HODEV64R	HODEV64R poly(A)-binding protein [Homo sapiens] >gi 1562511 poly(A)-binding protein [Homo sapiens] >sp P11940 PAB1_HUMAN POLYADENYLATE-BINDING PROTEIN 1 (POLY(A) BINDING PROTEIN 1).	gi 1562511	-	492	76	20	HODEV64	HODEV64 Lang, Panereas

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Pancreas, Colon	Panereas, Colon	Lung. Panereas	Lung, Pancreas, Prostate, Colon, Breast/Ovarian	Panereas, Colon
112CBD48	HCCMA82	HOEMK78	Н2СВ D13	нстмиы
76	94	\$6	001	86
95	94	95	100	86
499	383	329	461	477
71	m	m	156	-
gij3726.l	gi 189625	bbs 161346	gniP1D d1001118	pir A44266 A44266
precursor polypeptide (AA -21 to 782) [Homo sapiens] >pirlA35954[A35954 endoplasmin precursor - human >splP14625[ENPL_HUMAN ENDOPLASMIN PRECURSOR (94 KD GLUCOSE-REGULATED PROTEIN) (GRP94) (GP96 HOMOLOG) (TUMOR REJECTION ANTIGEN 1). Length = 803	HCCMA82R procarboxypeptidase B [Homo sapiens] >pir A42332 A42332 carboxypeptidase B (EC 3.4.17.2) precursor, pancreatic - human Length = 416	HOI:MK78R prostacyclin-stimulating factor, PGI2-stimulating factor, PSF [human, cultured diploid fibroblast cells. Peptide, 282 aa] [Homo sapiens] >pirJS50031[S50031 prostacyclin-stimulating factor - human >sp[Q16270]Q16270 PROSTACYCLIN-STIMULATING FACTOR. Length =	proteasome subunit C9 [Homo sapiens] >pirJS I 5972 SNHUC9 multicatalytic endopeptidase complex (EC 3 4.99.46) chain C9 - human >splP25789 PRC9_HUMAN PROTEASOME COMPONENT C9 (EC 3.4.99.46) (MACROPAIN SUBUNIT C9) (MULTICATALYTIC ENDOPEPTIDASE COMPLEX SUBUNIT	HCFMU61R protein-tyrosine kinase (EC 2.7.1.112) ZAP-70 - human Length = 619
H2CBD48R	HCCMA82R	HOI:MK78R	H2CBD13R	HCFMU6IR
714	715	716	717	718

HOSNE94 Lang, Panereas	HCROZ08 Lung, Pancreas. Colon	HHBEF47 Coton. Breast/Ovarian	HTXP131 Pancreas. Breast/Ovarian	HOEKC30 Lung, Pancreas. Breast/Ovarian
· %	00	*	88	46
€	001	*	84	94
466	218	330	286	151
2	M	_		7
gil181170	gi 37599	1387011	gi 972104	gi 36034
proteoglycan core protein [Homo sapiens] >pir[A45016]NBHUC8 decorin precursor - human >splP07585]PGSZ_HUMAN BONE PROTEOGLYCAN II PRECURSOR (PG-S2) (DECORIN) (PG40). >gi[1161226 decorin [Rattus norvegicus] {SUB 204-299} Length = 359	putative precursor (AA 1-304) [Homo sapiens] >gnl PID e224276 uracil-DNA-glycosylase, UNG1 [Homo sapiens] >pir(S05964 A60472 uracil-DNA glycosylase [EC 3) precursor - human >gnl\PID e1296296 MITOCHONDRIAL LOCALIZATION PEPTIDE [unidentified] (SUB 1-3	pyruvate dehydrogenase E1-alpha precursor [Homo sapieus] >pir[A60225]A60225 pyruvate dehydrogenase (lipoamide) (EC 1.2.4.1) alpha chain - bovine (fragment) {SUB 54-74} Length = 414	pyruvate kinase M2 [Sus scrofa] >splQ29582 Q29582 PYRUVATE KINASE M2 (EC 2.7.1.40) (PHOSPHOENOLPYRUVATE KINASE) (PHOSPHOENOL TRANSPHOSPHORYLASE) (FRAGMENT). Length = 108	HOEKC30R rhoC coding region (AA 1-193) [Homo sapiens] >gil407699 GTPase [Homo sapiens] >pirfS01029JTVHURC GTP-binding protein rhoC - human Length = 193
HOSNE94R	HCROZ08R	HIBEF47R	HT'XPI31R	HOEKC30R
912	720	121	722	723

Lung, Pancreas. Prostate, Colon. Breast/Ovarian	Lung, Pancreus. Colon, Breast/Ovarian	Lung. Breust/Ovarian	Lung, Pancrens, Colon	Lung, Panereas, Colon
H2LAV92	H2LA074	HKMMF85	HCLB227	H2LAVII
22	83	96	86	66
22	8	96	93	66
351	502	360	273	530
	359	-	61	126
gi 407423	gi 414587	gi 401845	8i 36128	gi 550015
H2LAV92R ribosomal protein [Homo sapiens] >gi 57078 ribosomal protein L38 [Rattus rattus] >pir S15658 R5RT38 ribosomal protein L38 - rat >pir S38385 S385 ribosomal protein L38 - human >gu PII) d 1026783 (AB007185) ribosomal protein L38 [Homo sapiens] {SUB 34-70}	H2LAO74R ribosomal protein L10 [Homo sapiens] >sp D1026771 D1026771 RIBOSOMAL PROTEIN L15 (FRAGMENT). {SUB 16-57} Length = 205	HKMMF85R ribosomal protein L18a [Homo sapiens] >gi 3702270 (AC005796) ribosomal protein L18a [Homo sapiens] >gnl PID d1029536 (AB007175) ribosomal protein L18a [Homo sapiens] {SUB 111-176} Length = 176	ribosomal protein L19 [Homo sapiens] >bbs 127872 ribosoinal protein L19 [human, breast cancer cell line, MCF-7, Peptide, 196 aa] [Homo sapiens] >gi 206726 ribosomal protein L19 [Rattus norvegicus] >gn PID[e218038 ribosomal protein L19 [Rattus norvegicus]	ribosomal protein L21 [Homo sapiens] >gi 984143 ribosomal protein L21 [Homo sapiens] >pir S55913 S55913 ribosomal protein L21, cyrosolic - human >sp D1026774 D1026774 RIBOSOMAL PROTEIN L21 (FRAGMENT). {SUB 124-154} Length = 160
H2LAV92R	H2LAO74R	HKMMF85R	HCLBZ27R	H2LAVIIR
	726	727	728	729

: : : :		0,2001.		į	;	ć	330	- - - -
ribosomal protein L27 [Ho ribosomal protein L27 [Ho ribosomal protein L27 (A/ norvegicus] >gi 62981 rib [Gallus gallus] >pir S0040 protein L27, cytosolic - ra	HIJACI F60R ribosomal protein L27 [Homo sapiens] >gij 115335 ribosomal protein L27 [Homo sapiens] >gij 57694 ribosomal protein L27 (AA 1 - 136) [Rattus norvegieus] >gij 62981 ribosomal protein L27 [Gallus gallus] >pir 500401 R5RT27 ribosomal protein L27, cytosolic - ra	81J388769	9	. 373	99	9	HBAGP60	Pancreas. Colon
HOEMJ56R ribosomal protein L2: >pirJSS5915 S55915 Length = 137	8 [Homo sapiens] ribosomal protein L28 - human	gi 550019	m	206	94	94	HOEMJS6	Lung, Colon. Breast/Ovarian
HASAF77R ribosomal protein L3 ribosomal protein L3 >gi[57115 ribosomal [Rattus norvegicus]> ribosomal protein L3 >pir[A26417]R58T31	ribosomal protein L31 [Sus scrofa] > gi 36130 ribosomal protein L31 (AA 1-125) [Homo sapiens] > gi 57115 ribosomal protein L31 (AA 1-125) Rattus norvegicus] > pir 505576 R5HU31 Rattus norvegicus] - pir 505576 R5HU31 ribosomal protein L31 - human > pir A26417 R5RT31 ribosomal protein L31 - rat	gnipiDje276436	-	381	22		HASAF77	Lung, Prostate. Colon. Breast/Ovarian
ribosomal protein L37 ribosomal protein L37 fluman, HeLa cells, P >gnl PID d1005426 ril sapiens >gi 57121 rib norvegicus}>	H2MAC95R ribosomal protein L37 {Homo sapiens} >bbs 172744 ribosomal protein L37 {C2-C2 zinc-finger-like} {human, HeLa cells, Peptide, 97 aa] [Homo sapiens] >gn PID 01005426 ribosomal protein L37 {Homo sapiens} >gi 57121 ribosomal protein L37 [Rattus norvegicus] >	gi 292441	67	4	79	67	Н2МАС95	Lung, Cołon. Breast/Ovarian
ribosomal protein L37 ribosomal protein L37 [human, HeLa cells, P >gnl[P1D]d1005426 rii sapiens] >gi[57121 rib norvegicus] >	ribosomal protein L37 [Homo sapiens] >bbs 172744 ribosomal protein L37 {C2-C2 zinc-finger-like} [human, HeLa cells, Peptide, 97 aa] [Homo sapiens] >gn PID d1005426 ribosomal protein L37 [Homo sapiens] >gi 57121 ribosomal protein L37 [Rattus norvegicus] >	gi 292441	-	363	001	100	HDPLP40	Lung, Pancreus, Breast/Ovarian

HOEMK92 Lang, Panereas. Breast/Ovarian	HABAD57 Lung, Pancreas	HLXNA52 Lung. Panereus	HWAFK82 Lung, Colon, Breast/Ovarian	H2CBL68 Lung, Panerens	HINTNEI7 Lung. Pancreus.
96	06	98 9	7 78	001	100
96	80	98	77	90	100
8	431	296	354	461	387
m	210	e	139	m	
gi 292439	gi 307385	gnllP1Dle121603	gi 710366	gil307391	gi 337501
HOEMK92R ribosomal protein L37a [Homo sapiens] >gi 36134 ribosomal protein L37a [Homo sapiens] >gi 57123 ribosomal protein L37a (AA 1 - 92) [Raitus rattus] >gi 312414 ribosomal protein L37a [Mus musculus] >pir S05014 R5RT37 ribosomal protein L37a - rat >pir S42109	HABAD57R ribosomal protein L4 [Homo sapiens] > pir[S39803 S39803 ribosomal protein L4 - human Length = 425	HLXNA52R ribosomal protein L4 [Rattus norvegicus] Length = 421	IIWAFK82R ribosomal protein L9 [Homo sapiens] >gni[PID]d1003911 'human homologue of rat ribosomal protein L9' [Homo sapiens] Length = 192	ribosomal protein S13 [Homo sapiens] >gi 488417 ribosomal protein S13 [Homo sapiens] >gn p10101422 ribosomal protein S13 [Homo sapiens] >gi 57730 ribosomal protein S13 [Rattus rattus] >pi 534109 534109 ribosomal protein S13, cytosolic - human >pir A3	ribosomal protein S17 [Homo sapiens] >gi[337503] S17 ribosomal protein [Homo sapiens]
HOEMK92R	HABAD57R	HLXNA52R	HWAFK82R	H2CBL68R	HNTNE17R
735	736	737	738	739	740

Lung, Panereas, Coton, Breast/Ovarian	Lung, Pancreas, Colon. Breast/Ovarian	Lung, Pancreus. Breast/Ovarian	Lung, Pancreas. Colon, Breast/Ovarian	Colon. Breast/Ovarian	Colon. Breast/Ovarian
HOSNG20	HCLBZ30	HBGNYII	HOEKC80	. НСНВМ70	HFCESS3
86	68	001	86	\$	98
7.6	68	001	86	52	80
357	244	334	376		165
- .	7	~	7	-	-
gi 337510	gi 1685071	gi 36150	gi 337733	gi 402483	gi 854328
HOSNG20R ribosomal protein S4X isoform [Homo sapiens] >gi[2791861 (AF041428) ribosomal protein s4 X isoform [Homo sapiens] >gi[200864 ribosomal protein S4 [Mus musculus] >gi[57135 ribosomal protein S4 (AA 1 - 263) [Rattus rattus] >gnl[P1D[d1002335 ribosomal protei	HCLBZ30R ribosomal protein S5 [Mus musculus] Length = 204	HBGNY11R ribosomal protein S8 [Homo sapiens] >gil57139 ribosomal protein S8 (AA 1-208) [Rattus norvegicus] >gil313298 ribosomal protein S8 [Mus musculus] >pir S01609 R3RT8 ribosomal protein S8 - rat >pir S42110 S42110 ribosomal protein S8 - mouse >pir S25022 S2502	HOEKC80R S19 ribosomal protein [Homo sapiens] >pir 152692 152692 ribosomal protein S19, cytosolic • human Length = 145	secretory protein [Homo sapiens] >gif940946 intestinal trefoil factor [Homo sapiens] >pirlA48284/A48284 intestinal trefoil factor 3 precursor - human >spiQ07654 ITF_HUMAN INTESTINAL TREFOIL FACTOR PRECURSOR (HP1.B). Length = 80	HFCESS3R semaphorin C [Mus musculus] >pir 148746 148746 semaphorin C - mouse (fragment) >spiQ62179 Q62179 SEMAPHORIN C (SEM C) (FRAGMENT). Length = 782
HOSNG20R	HCLBZ30R	HBGNYIIR	HOEKC80R	НСНВМ70R	HFCES53R
742	743	744	745	746	747

Lung, Colon, Breast/Ovariun	Lung. Colon	Pancreas, Colon	Lung, Pancreas, Breast/Ovariun	Lung, Panereas, Colon, Breast/Ovarian	Lung, Pancreis. Colon
HCRQC92	HAOAG75	HWAFE36	HBGOU57	HTXPF20	HCRMD09
8	100	100	27	***************************************	84
86	100	001	\$7	₹	98
278	418	127	314	549	460
м .	7	7		-	2
gi 338392	gi 347964	gi 458545	gil490094	gi 490094	gi 339548
spermidine/spermine N1-acetyltransferase [Homo sapiens] >gi[338346 spermidine/spermine N1-acetyltransferase [Homo sapiens] >splP21673/ATDA_HUMAN DIAMINE ACI:TYLTRANSFERASE (EC 2.3.1.57) (SPERMIDINE/SPERMINE N1-ACETYLTRANSFERASE) (SSAT) (PUTRESCINE ACETYLT	HAOAG75R TARBP-b gene product [Homo sapiens] Length = 277	TEGT gene product [Homo sapiens] >pir[138334]138334 TEGT (testis enhanced gene transcript) - human Length = 237	TIMP gene product [Homo sapiens] >gi 182483 prefibroblast collagenase inhibitor [Homo sapiens] >gi 189382 collagenase inhibitor [Homo sapiens] >gi 37183 precursor [Homo sapiens] >pir A93372 ZYHUEP metalloproteinase tissue inhibitor precursor - human >gi	TIMP gene product [Homo sapiens] >gi 182483 prefibroblast collagenase inhibitor [Homo sapiens] >gi 189382 collagenase inhibitor [Homo sapiens] >gi 37183 precursor [Homo sapiens] >pir A93372[ZYHUEP metalloproteinase tissue inhibitor I precursor • human >gi	HCRMD09R transforming growth factor-beta 1 binding protein precursor [Homo sapiens] >pir[A35626[A35626 transforming growth factor beta-1-binding protein - human Length = 1394
НС RQC92R	HAOAG75R	HWAFE36R	нвсои57R	HTXPF20R	HCRMD09R
748	749	750	751	752	753

754	HAJRB47R	triose-phosphate isomerase [Pan troglodytes] >gi]37247 triosephosphate isomerase [Homo sapiens] >gi]1200507 triosephosphate isomerase [Homo sapiens] >gi]339841 triosephosphate isomerase (EC 5.3.1.1) [Homo sapiens] >pir[\$29743]ISHUT triose-phosphate isomer	gil 76960	~	334	001	001	HAJRB47	Lung, Pancreas. Breast/Ovarian	
755	HABGB36R			9	251			HABGB36	Lung. Breast/Ovarian	
756	HADBF86R			m	158			HADBF%6	Lung, Colon	
757	HADDP09R			6	76			HADDP09	Lung, Pancreas, Colon, Breast/Ovarian	
758	HAGCY06R			7	28		-	HAGCY06	Panereas, Breast/Ovarian	
759	HAGDI75R			-	99			HAGDI75	Colon. Breast/Ovarian	
092	HAI:IBD47R			811	429			HAHBD47	Lung, Pancreus	
191	HAHCR61R			165	422			HAHCR61	Pancreas, Colon	
762	HAJAU22R			101	202			HAJAU22	Pancreas. Colon	
763	HAMGB62R		t	212	370			HAMGB62	Lung, Pancreas. Colon. Breast/Ovarian	
764	HANGC52R	-			86			HANGC52	Lung, Pancreas, Colon	
765	HAPCF30R			7	94			HAPCF30	Lung, Colon	
766	HAPPV45R			216	536			HAPPV45	Lung. Pancreas	
792	HAPQK 19R			200	415			FIAPQK19	Lung, Pancreas	
992	HAPRL82R			m	233			HAPRL82	Lung. Pancreas	
492	HAQBT45R			40	255			HAQBT45	Lung, Colon	
770	HAUALS6R			127	315			HAUAL\$6	Pancreas. Breast/Ovarian	

Panereas, Colon.	Breast/Ovarian Lung, Colon, Breast/Ovarian	Pancreas, Colon	Pancreas, Colon	Lung, Pancreas. Colon. Breast/Ovarian	Colon, Breast/Ovarian	Pancreas. Colon	Panereas, Colon	Lung, Pancreas,	Colon. Breast/Ovarian	Lung. Panereas	Panereas, Colon	Lung, Pancreus, Colon	Pancreas, Colon	Pancreas. Colon	Colon, Breast/Ovarian	Pancreas, Breast/Ovarian	Colon, Breast/Ovarian	Lung, Colon	Pancreas, Colon	Colon, Breast/Ovarian	Pancreus, Colon	Lung. Colon
HAUBR22	HBAFN19	HBGOK25	HBGRA76	HBGRB47	HBJAS24	HBJK105	HBKEC86	HBLGD42		HBPAF10	HCDBU02	HCDBU04	HCDDT61	HCEGY65	HCHAK80	нсним79	нснов92	HCL.BO01	HCQAN60	HCRAK70	HCRPC63	HCUDCS1
67	257	528	88	=	99	362	409	341		99	184	348	121	79	513	432	350	149	122	293	129	265
2	m _.	274	2	-	-	207	254	e		3	\$9	64	2	2	-	57	93	45	e	m	-	~
	·																					
HAUBR22R	HBAFN19R	HIBGOK25R	HBGRA76R	HBGRB47R	HBJAS24R	HBJK105R	HBKEC86R	HBLGD42R		HBPAF10R	HCDBU02R	HCDBU04R	HCDDT61R	HCEGY65R	HCHAK80R	HCHMW79R	HCHOB92R	HCLBOOIR	HCQAN60R	HCRAK70R	HCRPC63R	HCUDC51R
171	27.7	27.3	774.	27.5	776	ררר	778	779		780	781	782	783	784	782	786	787	788	789	790	161	792

793	HDPF140R	139	453	HDPF140	Lung, Pancreas, Breast/Ovarian
794	HI)PLP23R	_	141	HDPLP23	Pancreus, Colon, Breast/Ovarian
795	IIDPRZ54R	_	165	HDPRZ54	Colon, Breast/Ovarian
796	HE9DP46R	7	991	HE9DP46	Lung, Pancreas, Colon
797	HEGARI9R	361	534	HEGAR19	Lung, Colon
862	HFAU064R	27	137	HFAU064	Colon, Breast/Ovarian
799	HFIAL90R	186	308	HFIAL90	Lung, Colon.
800	нивефізя	218	514	ннвео12	Lung, Panereus
801	ннейска предвеждения преждения предвеждения прем предвеждения предвежд	2	127	ннеог94	Lung, Pancreas. Colon
802	HISCF76R	91	153	HISCF76	Pancreas, Colon
803	HJMAU64R	- .	207	HJMAU64	Lung, Colon
804	IIIPC125R	275	508	11JPC125	Lung, Panereas. Colon
805	HKBAC48R	369	542	HKBAC48	Lung, Panereas, Colon, Breast/Ovarian
908	HKBAD57R	165	341	HKBAD57	Lung, Pancreas
807	HKDBA91R	m	332	HKDBA91	Pancreas, Colon
808	HKGDB80R	ë.	224	HKGDB80	Lung. Colon
808	HLDNC95R	289	537	HLDNC95	Lung, Pancreas, Prostate, Colon
810	HMSNI52R	. 2	271	HMSN152	Lung. Pancreas
811	HODAYIGR	134	298	HODAY16	Colon. Breast/Ovarian
812	HODEA57R	586	471	HODEA57	Lung, Pancreas
813	HOEMO27R	_	09	НОЕМО27	Colon, Breast/Ovarian

814	HOEMO62R			73	ноемо62	Pancreas, Breast/Ovarian	
818	HOEMS18R	-		102	HOEMS18	Lung, Panereas. Colon, Breast/Ovarian	•
918	HOENUS3R	31	ν,	267	HOENUS3	Lung, Colon	
817	HOGAP33R			498	HOGAP33	Pancreas, Prostate, Breast/Ovarian	
818	HOSMV34R	124	4	327	HOSMV34	Lung, Pancreas, Breast/Ovarian	
618	HOSNF25R	405	\$	587	HOSNF25	Pancreas, Colon	
820	HOUHO32R	230	0	391	HOUH032	Lung, Colon	
821	HPIAC23R			286	HPIAC23	Lung. Breast/Ovarian	
822	HRAAD31R	311	\$	414	HRAAD31	Lung, Colon	
823	HRACR12R	2		100	HRACR12	Panereas, Colon	
824	HRADJ57R	2		142	HRADJ57	Lung, Colon	
825	HROAX48R	184	4	285	HROAX48	Pancreas, Colon	
826	HTAHR87R	369	6	491	HTAHR87	Lung, Pancreas	
827	H1TIO45R	-		288	HTTT1045	Colon. Breast/Ovarian	
828	HTWDH05R	 .		420	HTWDH05	Lung, Pancreas. Colon. Breast/Ovarian	
829	HUFDS13R	18		152	HUFDS13	Pancreas, Colon	
830	HUSZE86R	2		340	HUSZE86	Pancreas, Colon	
83	HUTHF75R	91	_	418	HUTHF75	Lung. Pancreas. Breast/Ovarian	
832	HWAFW07R			170	HWAFW07	Lung. Pancreas. Colon	
833	HWLIB82R	209	3	403	HWLIB82	Pancreas, Colon	
834	HWLLX91R	147		302	HWLLX91	Lung, Colon	
835	HWLMZ54R			120	HWLMZ54	Panereas, Colon	

					•	
Pancreas, Colon. Breast/Ovarian	Pancreas, Culon	Lung, Colon	Colon. Breast/Ovarian	Lung, Colon	Lung, Panereas. Colon	Pancreas, Colon
HMIAI78	HBGFJ39	НАМНН32	HAQBQ95	НАСНҮ58	HOSNE37	HWAFE41
	100			\$ 6	62	84
	001		•	%	89	84
319	153	123	202	1 1 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	231	208
.173	- '	- :	104		73	7 .
	gni P1D d1008821			gi 13004	gi 578710	bbs 155932
	unknown product specific to adipose tissue [Homo sapiens] >sp[Q15847]Q15847 HYPOTHETICAL 7.9 KD PROTEIN. Length = 76			HAGHYSRR URF I (NADH dehydrogenase subunit) [Homo sapiens] >gi337189 protein I [Homo sapiens] >pir[A00407]DNHUNI NADH dehydrogenase (ubiquinone) (EC 1.6.5.3) chain 1 - human mitochondrion (SGC1) >spiP03886]NU1M_HUMAN NADH-UBIQUINONE OXIDOREDUCTASE CHAIN I (EC 1.6	HOSNE37R URF 2 (NADH dehydrogenase subunit) [Homo sapiens] >gi[2052363 protein 2 [Homo sapiens] >gi[2582057 (AF014882) NADH dehydrogenase subunit 2 [Homo sapiens] >gi[2582061 (AF014884) NADH dehydrogenase subunit 2 [Homo sapiens] >gi[2582063 (AF014885) NADH dehydrogenase subunit 2 [Homo sapiens] >gi[2582063 (AF014885) NADH dehydr	HWAFE41R VDUP1=1,25-dihydroxyvitamin D-3 up-regulated [human, HL-60 promyelocytic leukemia cells, Pcptide, 391 aa] [Homo sapiens] Length = 391
HMIAI78R	HBGF139R	HAMHH32R	HAQBQ95R	HAGHY88R	HOSNE37R	HWAFE41R
836	837	838	839	840	- R	842

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The first column of Table I shows the "SEQ ID NO:" for each of the 842 cancer antigen polynucleotide sequences of the invention.

The second column in Table 1, provides a unique "Sequence/Contig ID" identification for each cancer associated sequence. The third column in Table 1, "Gene Name," provides a putative identification of the gene based on the sequence similarity of its translation product to an amino acid sequence found in a publicly accessible gene database, such as GenBank (NCBI). The great majority of the cDNA sequences reported in Table 1 are unrelated to any sequences previously described in the literature. The fourth column, in Table 1, "Overlap," provides the database accession no. for the database sequence having similarity. The fifth and sixth columns in Table 1 provide the location (nucleotide position nos. within the contig), "Start" and "End", in the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred ORF shown in the sequence listing as SEQ ID NO:Y. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the portion of SEQ ID NO:X delineated by the nucleotide position nos. "Start" and "End". Also provided are polynucleotides encoding such proteins and the complementary strand thereto. The seventh and eighth columns provide the "% Identity" (percent identity) and "% Similarity" (percent similarity) observed between the aligned sequence segments of the translation product of SEO ID NO:X and the database sequence.

The ninth column of Table 1 provides a unique "Clone ID" for a clone related to each contig sequence. This clone ID references the cDNA clone which contains at least the 5' most sequence of the assembled contig and at least a portion of SEQ ID NO:X was determined by directly sequencing the referenced clone. The reference clone may have more sequence than described in the sequence listing or the clone may have less. In the vast majority of cases, however, the clone is believed to encode a full-length polypeptide. In the case where a clone is not full-length, a full-length cDNA can be obtained by methods described elsewhere herein.

The tenth column of Table 1, "Tissue," provides the tissue source where each unique SEQ ID NO:X was found to be predominantly expressed.

Table 3 indicates public ESTs, of which at least one, two, three, four, five, ten, or more of any one or more of these public ESTs are optionally excluded from the invention.

SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing as SEQ ID NO:1 through SEQ ID NO:842) and the translated SEQ ID NO:Y

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(where Y may be any of the polypeptide sequences disclosed in the sequence listing as SEQ ID NO:843 through SEQ ID NO:1684) are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and decribed further below. For instance, SEQ ID NO:X has uses including, but not limited to, in designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the related cDNA clone contained in a library deposited with the ATCC. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y have uses that include, but are not limited to, generating antibodies which bind specifically to the cancer antigen polypeptides, or fragments thereof, and/or to the cancer antigen polypeptides encoded by the cDNA clones identified in Table I.

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Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing the related cDNA clone (deposited with the ATCC, as set forth in Table 1). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X.

The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC on:

5 Table 2

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ATCC Deposits	Deposit Date	ATCC Designation Number
LP01, LP02, LP03, LP04, LP05,	May-20-97	209059, 209060, 209061, 209062, 209063,
LP06, LP07, LP08, LP09, LP10,		209064, 209065, 209066, 209067, 209068,
LPII,		209069
LP12	Jan-12-98	209579
LP13	Jan-12-98	209578
LP14	Jul-16-98	203067
LP15	Jul-16-98	203068
LP16	Feb-1-99	203609
LP17	Feb-1-99	203610
LP20	Nov-17-98	203485
LP21	Jun-18-99	PTA-252
LP22	Jun-18-99	PTA-253
LP23	Dec-22-99	PTA-1081

each is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as shown in Table 5. These deposits are referred to as "the deposits" herein. The tissues from which the clones were derived are listed in Table 5, and the vector in which the cDNA is contained is also indicated in Table 5. The deposited material includes the cDNA clones which were partially sequenced and are related to the SEQ ID NO:X described in Table 1 (column 9). Thus, a clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Although the sequence listing lists only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to complete the sequence of the DNA included in a clone isolatable from the

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ATCC Deposits by use of a sequence (or portion thereof) listed in Table 1 by procedures hereinafter further described, and others apparent to those skilled in the art.

Also provided in Table 5 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

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Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-10 Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into E. coli strain XL-1 Blue, also available from Stratagene.

Vectors pSport1, pCMVSport 1.0, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., Focus 15:59 (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the cDNA contained in a deposited cDNA clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include, but are not limited to, preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

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Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the cDNA contained in the related cDNA clone in the deposit, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the related cDNA clone (See, e.g., columns 1 and 9 of Table 1). The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in a deposited library. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by the the dDNA in the related cDNA clone contained in a deposited library, are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the complement of the coding strand of the related cDNA clone contained in a deposited library.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence would unduly burden the disclosure of this application. Accordingly, for each "Contig Id" listed in the first column of Table 3, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described in the second column of Table 3 by the general formula of a-b, each of which are uniquely defined for the SEQ ID NO:X corresponding to that Contig Id in Table 1. Additionally, specific embodiments are directed to polynucleotide sequences excluding at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. for each Contig Id which may be

included in column 3 of Table 3. In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example.

Table 3.

Sequence/	General formula	Genbank Accession No.
Contig 1D 507291	Descending and descent	
507291	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 542 of SEQ ID	
	NO:1, b is an integer of 15 to 556, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:1, and where b is greater than	
500000	or equal to a + 14.	
508000	Preferably excluded from the present invention are	T40333, T41194, T66286, T66339,
	one or more polynucleotides comprising a nucleotide	T73997, T86453, T87207, R17614,
	sequence described by the general formula of a-b.	R19835, R43336, R45934, R48920,
	where a is any integer between 1 to 2648 of SEQ ID	R53521, R43336, R45934, R61813,
	NO:2, b is an integer of 15 to 2662, where both a and	R75928, R75937, H30115, H42959,
	b correspond to the positions of nucleotide residues	H39114, H43825, AA028010,
	shown in SEQ ID NO:2, and where b is greater than	AA028107, AA028148, AA031964,
1	or equal to a + 14.	AA032046, AA035668, AA190570,
		AA233781, AA461489, AA460726,
518325	Decfeed by and of face of	AA460898
J10323	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 324 of SEQ ID	
	NO:3, b is an integer of 15 to 338, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:3, and where b is greater than	
523111	or equal to a + 14.	
323111	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 799 of SEQ ID	
	NO:4, b is an integer of 15 to 813, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:4, and where b is greater than	,
26060	or equal to a + 14.	
526869	Preferably excluded from the present invention are	AA459771
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 887 of SEQ ID	
	NO:5, b is an integer of 15 to 901, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:5, and where b is greater than	
	or equal to a + 14.	
	Preferably excluded from the present invention are	H30209, H92182, W95693, W95692,
		AA196967
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 717 of SEQ ID	
	NO:6, b is an integer of 15 to 731, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:6, and where b is greater than	
	or equal to a + 14.	
		R14583, R93797, H52942, H75493,
	one or more polynucleotides comprising a nucleotide	H78857, W17094, W38705, W81551,
	sequence described by the general formula of a-b,	W90159, N90874, AA010244,

1	where a is any integer between 1 to 2760 of SEQ ID	AA029093. AA126501, AA147066
	NO:7. b is an integer of 15 to 2774, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:7, and where b is greater than	
	or equal to a + 14.	
537932	Preferably excluded from the present invention are	T91131, T84801, T85952, R59198,
1	one or more polynucleotides comprising a nucleotide	R59256, H43456, H59480, H79111,
	sequence described by the general formula of a-b,	N26560, N35676, N64506, N66078,
	where a is any integer between 1 to 2599 of SEQ ID	N76033, N78705, W07594, W70111,
	NO:8, b is an integer of 15 to 2613, where both a and	W70169, N90844, AA026910,
	b correspond to the positions of nucleotide residues	AA026911, AA057689, AA079631,
	shown in SEQ ID NO:8, and where b is greater than	AA079805, AA131257, AA136081,
	or equal to a + 14.	AA165115, AA210764, AA211886,
		AA232838, AA262352
540117	Preferably excluded from the present invention are	T49371, T49372, T49850, T61568,
Ì	one or more polynucleotides comprising a nucleotide	T64892, N39534, W57682, AA031859
	sequence described by the general formula of a-b,	, , , , , , , , , , , , , , , , , , , ,
	where a is any integer between 1 to 1087 of SEQ ID	
	NO:9, b is an integer of 15 to 1101, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:9, and where b is greater than	
	or equal to a + 14.	1
547710	Preferably excluded from the present invention are	R11154, R11155, R61204, R61205,
	one or more polynucleotides comprising a nucleotide	R82674, H06105, R88575, R88638,
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1359 of SEQ ID	H89977, H97031, N20224, W01143, W39387, W90318, W90788,
	NO:10, b is an integer of 15 to 1373, where both a	1
	and b correspond to the positions of nucleotide	AA001027, AA045864, AA045839,
	residues shown in SEQ ID NO:10, and where b is	AA070190, AA070357, AA070481,
		AA074270, AA099007, AA099084,
	greater than or equal to a + 14.	AA100370, AA112324, AA113319,
		AA158425, AA161510, AA171909,
		AA172133, AA173087, AA181768,
		AA188815, AA188874, AA190370,
551747	Proforably avaluded from the program investigation	AA226831, AA252143
001747	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	· ·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3790 of SEQ ID	
	NO:11, b is an integer of 15 to 3804, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:11, and where b is	
	greater than or equal to a + 14.	
552799	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2143 of SEQ ID	
	NO:12, b is an integer of 15 to 2157, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:12, and where b is	
	greater than or equal to a + 14.	
553243	Preferably excluded from the present invention are	H63183, W61352, AA151059
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1103 of SEQ ID	
	NO:13, b is an integer of 15 to 1117, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:13, and where b is	·

	greater than or equal to a + 14.	
553368	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 871 of SEQ ID	
	NO:14, b is an integer of 15 to 885, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:14, and where b is greater than	
	or equal to a + 14.	1
554349	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	İ
	sequence described by the general formula of a-b,	
,	where a is any integer between 1 to 1010 of SEQ ID	;
	NO:15, b is an integer of 15 to 1024, where both a	
	and b correspond to the positions of nucleotide	•
	residues shown in SEQ ID NO:15, and where b is	
	greater than or equal to a + 14.	
558491	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	l
	where a is any integer between 1 to 531 of SEQ ID	
	NO:16, b is an integer of 15 to 545, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:16, and where b is greater than	
	or equal to a + 14.	
558983	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 609 of SEQ ID	
	NO:17, b is an integer of 15 to 623, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:17, and where b is greater than	•
	or equal to a + 14.	
72943	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 545 of SEQ ID	
	NO:18, b is an integer of 15 to 559, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:18, and where b is greater than	
	or equal to a + 14.	
85892	Preferably excluded from the present invention are	
05072	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1341 of SEO ID	
	NO:19, b is an integer of 15 to 1355, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:19, and where b is	•
	greater than or equal to a + 14.	
89390	· · · · · · · · · · · · · · · · · · ·	T47629 T40402 T40020 T40020
U)J)U		T47628, T49403, T49829, T49830,
	one or more polynucleotides comprising a nucleotide	T50800, T50963, T51976, T55846,
		T55860, T55896, T55911, T58744,
		T58811, T58891, T59252, T59279,
	NO:20, b is an integer of 15 to 1280, where both a	T59293, T59615, T59690, T59727,
		T59826, T60434, T60514, T60584,
	residues shown in SEQ ID NO:20, and where b is	T61357, T40352, T62559, T62688,
	greater than or equal to a + 14.	T62839, T63122, T64603, T64640.

		T67682, T67756, T68181, T68439,
1		T68506. T68606, T68718, T68783,
1		T68839. T68849. T68976, T69049,
ł		T71223, T71347, T71509, T71853,
1		T71858, T71938, T72197, T72264,
		T72414, T72471, T72923, T73204,
i		T73259, T73283, T73446, T73607.
		T73621, T73645, T73713, T73744,
		T73772, T73796, T74114, T74545,
		T74599, T87829, T90307, T90394,
1		T91481, T92437, T92617, T81767,
		T82080, R27059, R27060, R31693,
		R31735, R50548, R50646, R64321,
		R64322, R75660, R75768, R75866,
1		R76038, R79765, R79766, H22209,
1		H24391, H25902, H27236, H28585,
		H29860, H29954, H41994, H42226,
1		H42298, H43069, H43893, H43934,
		R83465, R84983, R94905, R94988,
		R96360, R96403, R97059, R98674,
i		R98900, R99186, R99187, H50701,
ļ		H50801. H57754, H62182, H63649,
i	·	H63650, H64755, H64756, H69075,
		H70056, H70057, H70855, H70856,
		H71581, H75758, H75893, H80974,
ļ	· ·	H80975, H83141, H83142, H83271,
f		H85046, H84668, H91780, H92207,
	ļ	H92350, H94891, H94943, H94966,
		H95486, H99418, N52264, N58261,
		N74184, N77638, N81021, N92261.
1		N99137, W04350, W07850, W16893,
	·	W39467, W45038, W47174, W47433,
	·	W52853, W63782, W67635, W67759,
1		W67868, W67881, W93706, W94183,
		W96351, W96352, N89587, AA012898,
		AA019884, AA020863, AA025865,
		AA025866. AA056092, AA057434,
		AA070445, AA192155, AA192879,
	<u> </u>	AA226741, AA227477
596882	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1177 of SEQ ID	
	NO:21, b is an integer of 15 to 1191, where both a	•
	and b correspond to the positions of nucleotide	
j	residues shown in SEQ ID NO:21, and where b is	
	greater than or equal to a + 14.	
616289	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 839 of SEQ ID	
	NO:22, b is an integer of 15 to 853, where both a and	·
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:22, and where b is greater than	
	or equal to a + 14.	
622140	Preferably excluded from the present invention are	W39497, W52751, AA099814,
		AA128882. AA173072, AA226739

	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 460 of SEQ ID	
	NO:23. b is an integer of 15 to 474. where both a and	
1	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:23, and where b is greater than	
	or equal to a + 14.	
623566	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
ļ	sequence described by the general formula of a-b,	}
	where a is any integer between 1 to 2266 of SEQ ID	
	NO:24, b is an integer of 15 to 2280, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:24, and where b is	
	greater than or equal to a + 14.	
647714	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1047 of SEQ ID	
	NO:25, b is an integer of 15 to 1061, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:25, and where b is	
	greater than or equal to a + 14.	
647752	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
l	where a is any integer between 1 to 1558 of SEQ ID	
	NO:26, b is an integer of 15 to 1572, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:26, and where b is	
	greater than or equal to a + 14.	· ·
651774	Preferably excluded from the present invention are	T69901, T69949, T70775, R20554,
	one or more polynucleotides comprising a nucleotide	R33030, R33917, R48406, H58331,
	sequence described by the general formula of a-b,	H58720, H67041, H68124, H93586,
	where a is any integer between 1 to 1991 of SEQ ID	H94430, H94513, H97468, H99219,
	NO:27, b is an integer of 15 to 2005, where both a	N23459, N26334, N35428, N49203,
	and b correspond to the positions of nucleotide	N50256, N64246, N93349, W19550,
	residues shown in SEQ ID NO:27, and where b is	W19996, W25330, W73940, W77984,
	greater than or equal to a + 14.	W93791, W94028, N90424, AA025537,
		AA025680, AA025371, AA026317,
		AA026318, AA084549, AA086048,
		AA086130, AA098995, AA099068,
		AA115309, AA136486, AA151843,
		AA149689, AA148825, AA150406,
		AA150425, AA173377
651995	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1394 of SEQ ID	
	NO:28, b is an integer of 15 to 1408, where both a	}
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:28, and where b is	
	greater than or equal to a + 14.	
652156	Preferably excluded from the present invention are	T40364, R22492, R49907, R49908,
	one or more polynucleotides comprising a nucleotide	R62310, R62311, R65652, R67030,
	sequence described by the general formula of a-b,	R81699, R81700, H18589, H20024,
	where a is any integer between 1 to 903 of SEQ ID	H20099, H20123, H20797, H22404,
	NO:29, b is an integer of 15 to 917, where both a and	H22615, H25816, H27051, H42294,

	b correspond to the positions of nucleotide residues	MAA927 MA9661 MELA22 MELACE
	shown in SEQ ID NO:29, and where b is greater than	H44827, H49661, H51422, H51465,
	or equal to a + 14.	
	or equal to a 1 14.	H93528, H93860, H96113, H96114,
		N22715, N31188, N33831, N54495,
		N70601, N70623, N76607, N78626,
		W04920, W05505, W07305, W15350,
		W39442, W60859, W60860. W72726,
		W76452, AA017463, AA024543,
		AA024544, AA026421, AA026498,
		AA027270, AA034429, AA046316,
		AA046142, AA053920, AA056230,
		AA063244, AA062885, AA085305,
		AA128171, AA126216, AA149890,
		AA150552, AA187825, AA188597,
		AA417004, AA417190
653010	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 563 of SEQ ID	
	NO:30, b is an integer of 15 to 577, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:30, and where b is greater than	
	or equal to a + 14.	
655904	Preferably excluded from the present invention are	T61561, T90265, T90707, R09280,
	one or more polynucleotides comprising a nucleotide	R17627, R43348, R54854, R54658,
	sequence described by the general formula of a-b,	H20872, H27229, H64571, H64673,
	where a is any integer between 1 to 2045 of SEQ ID	H64571, N47495, N54722, N75461,
	NO:31, b is an integer of 15 to 2059, where both a	W73679, AA010711, AA010712,
	and b correspond to the positions of nucleotide	AA082107, AA130516, AA132052,
		AA132156, AA147852, AA147908,
		AA148276, AA148277, AA181933,
		AA187549, AA187845, AA186675,
		AA188310, AA193212
657852	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	<u>.</u>
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 535 of SEQ ID	
	NO:32, b is an integer of 15 to 549, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:32, and where b is greater than	
	or equal to a + 14.	
566414	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 827 of SEQ ID	
	NO:33, b is an integer of 15 to 841, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:33, and where b is greater than	
	or equal to a + 14.	
67847		T47000 T47010 T55133 75533
,,,,,,,,		T47009, T47010, T55133, T55301,
		T57663, T57702, T59664, T59797,
	sequence described by the general formula of a-b,	T59800, T49370, T72020, T26631,
	where a is any integer between 1 to 849 of SEQ ID	R22343, R46325, R48879, R50151,
	NO:34, b is an integer of 15 to 863, where both a and	R50204, R55208, R71485, R71535,
	b correspond to the positions of nucleotide residues	R72144, R72362, R72553, R74062,
	shown in SEQ ID NO:34, and where b is greater than	11338/, H1616/, H18121, H20172,
	or equal to a + 14.	H20361, H22514, H40774, H40775,

		H42435. H42865. H43100. H43164,
		H45140. H45441. H46013. H46083,
į		H46159, R97084, R97131, H56498,
		H60260, H60567, H67238, H71802,
İ		H77325, H77338, H81556, H87775,
ŀ		H87825. H91889. H92057. H93187,
		H96056, H96420, H81556, H99575,
1		N21484, N23829, N24221, N26831,
1		N27079, N27278, N27582, N30213,
Ì		N30255, N31642, N31989, N31996,
		N32655, N32790, N35515, N38983,
		N39859, N40012: N40488, N41792,
1		N41978, N54988. N57097, N70071,
1		N77176, N78930, N80037, N80573,
		N81058, N92768, N93810, W07000,
ŀ		W07659, W07868, W44961, W44962,
		W58175, W58263. W58182,
	•	AA001206, AA017579, AA026640,
		AA026706, AA057605, AA058758,
		AA082491, AA084088, AA086460,
	<u>'</u>	AA100968, AA112029. AA121337,
		AA121500, AA130704, AA130790,
	·	
		AA152420, AA156094, AA156123,
1		AA181929, AA182575, AA182617,
		AA186931, AA195982, AA253952,
		AA283976, AA426098, AA425122, AA428823, AA429359
670188	Preferably excluded from the present invention are	MA428823, MA429339
0.0.00	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1216 of SEQ ID	
	NO:35, b is an integer of 15 to 1230, where both a	ļ
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:35, and where b is	
1	greater than or equal to a + 14.	
670279	Preferably excluded from the present invention are	T50781, T51265, T55324, T56327
0.02.3	one or more polynucleotides comprising a nucleotide	130/61, 131203, 133324, 136327
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 626 of SEQ ID	
	NO:36, b is an integer of 15 to 640, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:36, and where b is greater than	
	or equal to a + 14.	
670729	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 583 of SEQ ID	
l	NO:37, b is an integer of 15 to 597, where both a and	
!	b correspond to the positions of nucleotide residues	. ,
	shown in SEQ ID NO:37, and where b is greater than	
1	or equal to a + 14.	
674123	Preferably excluded from the present invention are	
0/4123	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 610 of SEQ ID	i
	NO:38, b is an integer of 15 to 624, where both a and	
	b correspond to the positions of nucleotide residues	
<u> </u>	lo correspond to the positions of nucleotide residues	L

	shown in SEQ ID NO:38, and where b is greater than	<u> </u>
	or equal to a + 14.	
676496	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1015 of SEQ ID	
	NO:39, b is an integer of 15 to 1029, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:39, and where b is	
	greater than or equal to a + 14.	
678162	Preferably excluded from the present invention are	T40233, T40521, T41098, T47133,
	one or more polynucleotides comprising a nucleotide	T47529, T49156, T49157, T51636,
	sequence described by the general formula of a-b,	T55352, T55402, T55422, T57649,
	where a is any integer between 1 to 1093 of SEQ ID	T59314, T62530, T62806, T62954,
	NO:40, b is an integer of 15 to 1107, where both a	T72271, T73592, T89655, T78884,
	and b correspond to the positions of nucleotide	R19194, R89249, R93164, H57861,
	residues shown in SEQ ID NO:40, and where b is	H93645, N22493, N26661, N32984,
	greater than or equal to a + 14.	N63146, N66448, N67443, N69984,
		N72141, N77952, N78933, N81091,
		N95826, W02074, W24850, W24972,
		W38365, W44897, W57997, W58080,
		W65414, W65435, W74634,
		AA007562, AA009767, AA022918, AA022939, AA025169, AA029717,
		AA029656, AA032096, AA040581,
		AA046091, AA070493, AA070646.
	•	AA070707, AA071405, AA071414,
		AA074752, AA075706, AA075696,
		AA079282, AA085620, AA100126,
	·	AA126795, AA128838, AA136579,
		AA143069, AA143200, AA146637,
		AA147370, AA147705, AA156001,
		AA157342, AA161090, AA164798,
*		AA179749, AA187235, AA188048,
		AA187029, AA188384, AA192271,
		AA196973, AA235468, AA243180.
		AA459416, AA459642
578248	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1037 of SEQ ID	
	NO:41, b is an integer of 15 to 1051, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:41, and where b is	
83668	greater than or equal to a + 14. Preferably excluded from the present invention are	T40540 T40550 T40500 T40015
0000	one or more polynucleotides comprising a nucleotide	T49549, T49550, T49700, T49912,
	sequence described by the general formula of a-b,	T49937, T50912, T51558, T53285,
	where a is any integer between 1 to 2178 of SEQ ID	T53375, T53376, T53721, T54314,
	NO:42, b is an integer of 15 to 2192, where both a	T54840, T55217, T56413, T99069, T99669, R01522, R31653, R32820,
		R32921, R35743, R50997, R64077,
		R65723, R69349, R71009, R72798,
		R72824, R76854, R77142, R79240,
		R79511, R80194, R80295, R81155,
		H39823, H39824, R84909, R85592,
		R91193, H50793, H52341, H53594,
	1	H53916, H92997, N26572, N32090,

		N32406, N34179, N36271, N45401, N49216, N50267, N67233, N67568, N72254, N75478, N93355, N94504, W00543, W05288, W05816, W23954, W24625, W24650, W25354, W49666, W52302, AA121852, AA121851, AA128593, AA128712, AA136731, AA136688, AA167235, AA167584, AA173693, AA176648, AA176804, AA179999, AA181456, AA181457, AA256158, AA256215, AA256247, AA458729, AA458778, AA464936, AA464937
693172	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 339 of SEQ ID NO:43, b is an integer of 15 to 353, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.	T49005, T50129, T54766, T59468, T71241, T89633, R66699, R67578, H25853, H26090, H41256, H43182, H45273, N58288, N95319, AA054338, AA057604, AA084261
694303	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3476 of SEQ ID NO:44, b is an integer of 15 to 3490, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.	
695042	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 767 of SEQ ID NO:45, b is an integer of 15 to 781, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.	
699799.	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1417 of SEQ ID NO:46, b is an integer of 15 to 1431, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:46, and where b is greater than or equal to a + 14.	T50599, R25615, R31078, R68513, R70896, R75848, R76864, R76865, H01087, H26949, H63077, H75713, H75642, H95014, H98885, N24938, N33815, N47174, N47897, N51152, N53997, N59590, N62387, N63017, N67836, N69948, N78655, N79355, N94343, N98329, W01767, W03440, W15144, W19292, W25534, W37911, W42857, W42912, W48630, W72791, W76438, W81113, W80546, W80525, W80526, W84575, W84645, AA010674, AA011261, AA026981, AA031662, AA039737, AA039810, AA040524, AA040523, AA046308, AA046396, AA099365, AA101915, AA129310, AA129354, AA131951, AA186409
702216	Preferably excluded from the present invention are	T64167, T64355, T68409, T68475, T73691, T73717, T97735, T97840,

703015	sequence described by the general formula of a-b. where a is any integer between 1 to 1899 of SEQ ID NO:47, b is an integer of 15 to 1913, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1747 of SEQ ID NO:48, b is an integer of 15 to 1761, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is	T98899. T99491. R00460. R01214. R01326. H45786, R93124. R96609, H61118. H61119. H61454. H62460, H64003. H64052. H91078. H91378, N58480, N64695, N65991. N74260, N78070, N79244. N91708. N95101, W03761, W04301, N90479, AA130077, AA130076. AA152275, AA150441 R72819, R73270, H43839. W47195, W52204, AA242894, AA424584, AA424629
706391	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 942 of SEQ ID	T48974, H26922, H30342, H44743, H45233, R88178, H81778, H92363, N29006, N44860, N46515, AA079547, AA158434, AA160590, AA428285
	NO:49, b is an integer of 15 to 956, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.	
706892	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 549 of SEQ ID NO:50, b is an integer of 15 to 563, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:50, and where b is greater than or equal to a + 14.	·
706924	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3201 of SEQ ID NO:51, b is an integer of 15 to 3215, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.	T68892, T68966, T75421, R15205, R16398, R41650, R42339, R52995, R52996, R41650, H12000, H16753, H16861, H27652, H27653, H27982, H28497, H29323, H29416, H85752, H98511, N22580, N24339, N28586, N42727, N50084, N75803, N78815, W07245, W21306, W23840, W57924, W58128, W72277, W76304, W86460, AA002243, AA002080, AA025565, AA025683, AA026606, AA026718, AA150696, AA150801
707642	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 612 of SEQ ID NO:52, b is an integer of 15 to 626, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.	
710369	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 906 of SEQ ID NO:53, b is an integer of 15 to 920, where both a and	T48815, T60685, T91108, T99835, AA150217, AA157340, AA157240, AA171947

	b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.	
710026	Preferably excluded from the present invention are	
718826		
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	1
	1 1	
٠	where a is any integer between 1 to 1076 of SEQ ID	
	NO:54, b is an integer of 15 to 1090, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:54, and where b is	
710700	greater than or equal to a + 14.	T47380, T47538, T47539, T53445,
119790	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	T53446, T54910, T55077, T59959,
	sequence described by the general formula of a-b,	T60032, T62504, T62649, T63049,
	where a is any integer between 1 to 1450 of SEQ ID	T63297, T63382, T65688, T71591,
	NO:55, b is an integer of 15 to 1464, where both a	[771742, T93094, T93187, T94131,
	and b correspond to the positions of nucleotide	T94222, T91210, T84959, T99044,
	residues shown in SEQ ID NO:55, and where b is	T99045, R26119, R26148, R33224, R35866, R36526, R53923, R53924,
	greater than or equal to a + 14.	
		R69596, R69684, R76209, R76210,
		R79249, R79521, H03427, H03507, H12529, H13501, H19016, H19310,
	·	H21587, H21652, H21653, H30119,
		H39693, H42698, H46635, R93371,
		R98210, R99855, H54120, H54786,
		H54837, H58991, H65355, H65566,
		H67613, H72632, H74102, H95312,
		N48235, N58029, N64226, N66907,
		N70763, N78303, N93848, N94316,
		N95432, N98433, W01816, W02218,
		W05772, W21419, W24044, W24297,
		W30823, W32382, W37228, W37317,
		W40321, W42528, W46445, W49731,
		W51944, W53011, W53012, W60051,
		W60129, W60154, W68332, W68216,
		W72730, W74593, W92813, W93310,
		AA010985, AA011307, AA031435,
	·	AA035708, AA037040, AA053073,
		AA053374, AA055567, AA069724,
		AA069690, AA069682, AA069900,
		AA069951, AA070693, AA071421, AA074606, AA075555, AA075673,
	1	
		AA075544, AA081017, AA081251,
		AA081428, AA082119, AA082022, AA082213, AA082241, AA082247,
		AA082400, AA082365, AA082438,
		AA082679, AA083225, AA083266,
		AA083508, AA083411, AA083637,
		AA084202, AA099623, AA102015,
		AA099659, AA100102, AA100163,
		AA100429, AA100430, AA100455,
		AA100456, AA100711, AA100764,
		AA100906, AA100919, AA100963,
•		AA101118, AA102494, AA101184,
		AA112123, AA122359, AA122360,
		AA126882, AA127103, AA128195, AA128674, AA128686, AA128741,

		•
	T	AA128747, AA128785, AA133488.
1		AA133489, AA130006, AA130007.
1		AA134211, AA130492, AA130507,
1		AA134345, AA134346, AA134457,
1		AA134458, AA134461, AA134462,
		AA130907, AA131020, AA131973,
		AA132141, AA132493, AA132601,
		AA134904, AA135121, AA135182,
1		AA135348, AA136318, AA143066,
		AA143256, AA143278, AA143386,
		AA146650, AA146835, AA146836,
		AA146860, AA146861, AA146870.
		AA146871, AA146918, AA147716,
		AA147707, AA147868, AA148130,
Ì		AA148090, AA148091, AA152422,
		AA148435, AA148867, AA148492,
		AA148702, AA151453, AA151452.
1		AA151828, AA155801, AA155886,
1		AA156025, AA156044, AA156053,
1		AA156155, AA156222, AA157080,
1		AA157168, AA157325, AA157423,
		AA157434, AA157471, AA157605,
	·	AA157631, AA157546, AA157775,
1		AA157826, AA158157, AA158273,
		AA158888, AA158887, AA159153,
1	1	AA159250, AA160104, AA159856,
		AA161278, AA161301, AA160817,
		AA164741, AA165616, AA165606,
		AA173037, AA173038, AA176229,
		AA176317, AA179185, AA179190,
		AA179200, AA181043, AA181262,
1		AA181342, AA181834, AA181989,
		AA182794, AA187247, AA187342,
l.		AA187379, AA187470, AA187528,
		AA187740, AA187911, AA188028,
1		AA186378, AA186424, AA186441,
		AA186442, AA186568, AA186653,
		AA186661, AA186703, AA186910,
		AA187081, AA187087, AA187078,
1		AA187135, AA188313, AA188330,
		AA188342, AA190473, AA193219
720222		AA056718, AA428747
1	one or more polynucleotides comprising a nucleotide	
İ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 971 of SEQ ID	·
į	NO:56, b is an integer of 15 to 985, where both a and	
i	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:56, and where b is greater than	
	or equal to a + 14.	
724033		N50855, AA076233, AA076232
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1232 of SEQ ID	
	NO:57, b is an integer of 15 to 1246, where both a	
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:57, and where b is	
	greater than or equal to a + 14.	

724767	Preferably excluded from the present invention are	
ĺ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1952 of SEQ ID	
	NO:58. b is an integer of 15 to 1966, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:58, and where b is	
	greater than or equal to a + 14.	
727065	Preferably excluded from the present invention are	T26554, R31862, R31869, R67140,
	one or more polynucleotides comprising a nucleotide	R70861, H00137, H23051, H23350,
	sequence described by the general formula of a-b,	H60670, N28391, N28646, AA081571
	where a is any integer between 1 to 1597 of SEQ ID	
	NO:59, b is an integer of 15 to 1611, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:59, and where b is	
	greater than or equal to a + 14.	
727246	Preferably excluded from the present invention are	
1,2,240	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 1835 of SEQ ID	
1		
Ì	NO:60, b is an integer of 15 to 1849, where both a	·
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:60, and where b is	
707030	greater than or equal to a + 14.	
727932	Preferably excluded from the present invention are	
Ì	one or more polynucleotides comprising a nucleotide	
Į	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 219 of SEQ ID	
	NO:61, b is an integer of 15 to 233, where both a and	
	b correspond to the positions of nucleotide residues	•
	shown in SEQ ID NO:61, and where b is greater than	
	or equal to a + 14.	
731167	Preferably excluded from the present invention are	
ļ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	<u> </u>
	where a is any integer between 1 to 2319 of SEQ ID	
	NO:62, b is an integer of 15 to 2333, where both a	
l	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:62, and where b is	
	greater than or equal to a + 14.	
732514	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
}	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1456 of SEQ ID	
	NO:63, b is an integer of 15 to 1470, where both a	1
!	and b correspond to the positions of nucleotide	
· ·	residues shown in SEQ ID NO:63, and where b is	
	greater than or equal to a + 14.	
734080	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 925 of SEQ ID	
	NO:64, b is an integer of 15 to 939, where both a and	·
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:64, and where b is greater than	
	or equal to a + 14.	
734288	Preferably excluded from the present invention are	
137200	p reservoiry excluded from the present invention are	

730449	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2054 of SEQ ID NO:65, b is an integer of 15 to 2068, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.	T53676 T53677 T54741 T55955
739448	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1377 of SEQ ID NO:66, b is an integer of 15 to 1391, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.	T53676, T53677, T54741, T55855, T55906, T56935, T57622, T58975, T58979, T61059, T61143, T90498, T90594, T93775, R07734, R07735, R40067, R75954, R75978, R76790, R76809, R77290, R77315, R77348, R79433, R79434, R97814, H50168, H70091, H77406, H80889, H82088, H82195, N33576, N39028, N48219, N49421, N52598, N66328, N67208, N73788, N78932, N92856, N99411, W07071, W17213, W24422, W25582, W47407, W47574, W49651, W49725, W68140, W68467, AA025829, AA025972, AA074731, AA074835, AA075316, AA081368, AA081369, AA082652, AA082810, AA101054, AA102495, AA115718, AA115719, AA127079, AA127080, AA127200, AA127199, AA128645, AA128813, AA133732, AA130465, AA130466, AA132111, AA143233, AA143289, AA146780, AA147706, AA148134, AA151491, AA157062, AA157046, AA157630, AA165124, AA165123, AA164625, AA165420, AA165583, AA173407, AA173462, AA179910, AA179911, AA180198, AA181087, AA181556, AA182450, AA182951, AA186670, AA188289, AA192925, AA193075, AA464823
739668	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 645 of SEQ ID NO:67, b is an integer of 15 to 659, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.	
	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2967 of SEQ ID NO:68, b is an integer of 15 to 2981, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:68, and where b is greater than or equal to a + 14.	
741560	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	

		·
	where a is any integer between 1 to 589 of SEQ ID	
	NO:69, b is an integer of 15 to 603, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:69, and where b is greater than	
	or equal to a + 14.	
742543	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1087 of SEQ ID	1
	NO:70, b is an integer of 15 to 1101, where both a	. <mark> </mark>
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:70, and where b is	
	greater than or equal to a + 14.	
742831	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 700 of SEQ ID	
	NO:71, b is an integer of 15 to 714, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:71, and where b is greater than	
	or equal to a + 14.	
745327	Preferably excluded from the present invention are	, i
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2876 of SEQ ID	
	NO:72, b is an integer of 15 to 2890, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:72, and where b is	
	greater than or equal to a + 14.	
745695	Preferably excluded from the present invention are	T56303, T58644, T58694, R48815,
	one or more polynucleotides comprising a nucleotide	R48816, R68140, R74376, R78015,
	sequence described by the general formula of a-b,	R81014, H00852, H01233, H17193,
~	where a is any integer between 1 to 2474 of SEQ ID	H17969, H25101, H27005, H30607,
	NO:73, b is an integer of 15 to 2488, where both a	H41236, H42218, H42290, H42904,
	and b correspond to the positions of nucleotide	H42977, H45271, H45342, R83816,
	residues shown in SEQ ID NO:73, and where b is	R98855, R98939, H53696, H62059,
	greater than or equal to a + 14.	H82544, H83097, N40713, N92791,
		W19377, AA025571, AA053695,
		AA053675, AA069167, AA069166,
		AA076604, AA076603, AA079426,
. •		AA100088, AA099771, AA130265,
		AA158402, AA179641, AA235643,
		AA253454, AA250758, AA458951,
		AA458978, AA459194, AA419280,
		AA419329, AA425117, AA430664
750316	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 697 of SEQ ID	
	NO:74, b is an integer of 15 to 711, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:74, and where b is greater than	·
	or equal to a + 14.	
750522	Preferably excluded from the present invention are	
-	one or more polynucleotides comprising a nucleotide	i e
		1
	sequence described by the general formula of a-b, where a is any integer between 1 to 892 of SEQ ID	

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	NO:75. b is an integer of 15 to 906, where both a and	
}	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:75, and where b is greater than	,
750502	or equal to a + 14.	
750583	Preferably excluded from the present invention are	·
İ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 257 of SEQ ID	
	NO:76, b is an integer of 15 to 271, where both a and b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:76, and where b is greater than	
	or equal to a + 14.	
751020	Preferably excluded from the present invention are	N80268, N95387, W57806, W63590,
751020		AA182782, AA187759, AA199806,
	sequence described by the general formula of a-b,	AA262640, AA262111, AA262106.
	where a is any integer between 1 to 659 of SEQ ID	AA460214
	NO:77, b is an integer of 15 to 673, where both a and	101400214
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:77, and where b is greater than	
	or equal to $a + 14$.	
752196	Preferably excluded from the present invention are	R67541
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 353 of SEQ ID	
	NO:78, b is an integer of 15 to 367, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:78, and where b is greater than	
	or equal to a + 14.	
753084	Preferably excluded from the present invention are	T93791, T93840, R77826, R78199,
		R99272, H54274, H65600, H67128,
		H75533, H75532, H81433, N57836,
		N58786, N72699, N77475, W02480,
	NO:79, b is an integer of 15 to 1344, where both a	W78743, W80625, W90276,
/	and b correspond to the positions of nucleotide	AA007397, AA127528, AA127529,
	residues shown in SEQ ID NO:79, and where b is	AA130419, AA147733, AA150095,
754057	greater than or equal to a + 14.	AA195008, AA195060
754957	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3734 of SEQ ID NO:80, b is an integer of 15 to 3748, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:80, and where b is	
]	greater than or equal to a + 14.	
756557	Preferably excluded from the present invention are	
120221	one or more polynucleotides comprising a nucleotide	
ľ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1877 of SEQ ID	
	NO:81, b is an integer of 15 to 1891, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:81, and where b is	
	greater than or equal to a + 14.	
756712	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1940 of SEQ ID	
	NO:82, b is an integer of 15 to 1954, where both a	

	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:82, and where b is	
	greater than or equal to a + 14.	<u> </u>
757414	Preferably excluded from the present invention are	T49651, T49652, T92946, T93013.
	one or more polynucleotides comprising a nucleotide	H02307, H02419, N42072, AA169576
l	sequence described by the general formula of a-b.	
İ	where a is any integer between 1 to 922 of SEQ ID	j 1
i	NO:83, b is an integer of 15 to 936, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:83, and where b is greater than	
	or equal to a + 14.	
757614	Preferably excluded from the present invention are	T93709, T96172, H00439, H00480.
	one or more polynucleotides comprising a nucleotide	R85176, H51264, H51834, H53645,
	sequence described by the general formula of a-b.	H57470, H57991, H73334, N33138.
l	where a is any integer between 1 to 1499 of SEQ ID	N42318, N94987, AA028955,
Ì	NO:84, b is an integer of 15 to 1513, where both a	AA081550, AA082013, AA113225,
!	and b correspond to the positions of nucleotide	AA113810, AA133619, AA133522,
1	residues shown in SEQ ID NO:84, and where b is	
ĺ		AA132699, AA132810, AA151877,
	greater than or equal to a + 14.	AA149662, AA157324, AA157422,
		AA159905, AA165014, AA165442,
		AA165443, AA167837, AA166621,
		AA166924, AA195339, AA195338, AA252790
757815	Preferably excluded from the present invention are	AA232790
(10101)	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1284 of SEQ ID	
	NO:85, b is an integer of 15 to 1298, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:85, and where b is	
750070	greater than or equal to a + 14.	
759878	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1995 of SEQ ID	
	NO:86, b is an integer of 15 to 2009, where both a	
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:86, and where b is	
	greater than or equal to a + 14.	
760227	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 520 of SEQ ID	
	NO:87, b is an integer of 15 to 534, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:87, and where b is greater than	
	or equal to a + 14.	
760312	Preferably excluded from the present invention are	·
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 4288 of SEQ ID	
	NO:88, b is an integer of 15 to 4302, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:88, and where b is	
	greater than or equal to a + 14.	
766051	Preferably excluded from the present invention are	T57753, T60650, R11036, R11084,
	one or more polynucleotides comprising a nucleotide	R00826, R01482, H87221, N25112

	sequence described by the general formula of a-b.	N33451. N42424, N47338, N48186,
	where a is any integer between 1 to 2768 of SEQ ID NO:89, b is an integer of 15 to 2782, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.	N62628. N68902, N71490, N78399, N99533. W16943, W78948, W85915, W95743, N89568, AA039230, AA039231, AA047564, AA047582, AA047702, AA047752, AA120926, AA126453, AA135549, AA135529,
767593	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1023 of SEQ ID NO:90, b is an integer of 15 to 1037, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.	AA429718 T51635, T57709. T61468, T63793, T63818. T92894, T92984. T94396, T75475, T75508, T87575, T79848, T85949. R25644, R27489. R70702, R78772. H44836, H44835, R84349, R86157, R89703, R99494, H48567, H48836, H57859, H83579, H86373, H86690. H88284, H97937, H98241, H99117, H99249, N24363, N24573, N26374, N27129, N31662, N36546, N40064, N45098, N45108, N53503, N59526, N63219, N64179, N64178, N66660. N70536, N72298, N98943, W02894, W19364, W60295, W60386, W72691, W77806, W93582, W93631, W92326, W92382, N90765, AA001997, AA013356, AA017023, AA017221, AA018780, AA026639, AA026705, AA029569, AA029496. AA029736, AA035387, AA035694, AA044958, AA055558, AA063564. AA100726, AA100744, AA134118, AA130301, AA151965, AA233192, AA253060, AA253117
768053	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1038 of SEQ ID NO:91, b is an integer of 15 to 1052, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.	
768055	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1220 of SEQ ID NO:92, b is an integer of 15 to 1234, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.	T68053, R09316, R09788, T84929, R24826, R66259, R68879, R80029, H00967, H89841, H96162, N39802, N44634, N68319, N70487, N71145, N72732, W01594, W52285, W73342, W85800, AA022906, AA022975, AA031962, AA032044, AA032163, AA037604, AA043694, AA043695, AA044134, AA074287, AA081041, AA081042, AA082218, AA082461, AA082475, AA083977, AA100460, AA155926, AA167365, AA171958, AA173534, AA187036, AA224429
769685	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1557 of SEQ ID	-

	NO:93. b is an integer of 15 to 1571, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:93, and where b is	
	greater than or equal to a + 14.	·
771920	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	·
1	where a is any integer between 1 to 1858 of SEQ ID	i i
	NO:94, b is an integer of 15 to 1872, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:94, and where b is	
	greater than or equal to a + 14.	
772790	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
ļ	sequence described by the general formula of a-b,	,
	where a is any integer between 1 to 1502 of SEQ ID	
	NO:95, b is an integer of 15 to 1516, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:95, and where b is	
	greater than or equal to a + 14.	
772916	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1756 of SEQ ID	
	NO:96, b is an integer of 15 to 1770, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:96, and where b is	1
	greater than or equal to a + 14.	
773225	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 924 of SEQ ID	
	NO:97, b is an integer of 15 to 938, where both a and	•
	b correspond to the positions of nucleotide residues	
1	shown in SEQ ID NO:97, and where b is greater than	
	or equal to a + 14.	
773632	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
İ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 297 of SEQ ID	
1	NO:98, b is an integer of 15 to 311, where both a and	
]	b correspond to the positions of nucleotide residues	
1	shown in SEQ ID NO:98, and where b is greater than	
	or equal to a + 14.	
774364	Preferably excluded from the present invention are	W01405, AA172322
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 606 of SEQ ID	
	NO:99, b is an integer of 15 to 620, where both a and	
	b correspond to the positions of nucleotide residues	
	shown in SEQ ID NO:99, and where b is greater than	
	or equal to a + 14.	
775355 .	Preferably excluded from the present invention are	T49285, T61774, T68350, T68396,
İ	one or more polynucleotides comprising a nucleotide	T94414, T69842, T81078, R01216,
	sequence described by the general formula of a-b,	R05674, R21522, R21626, R23745,
	where a is any integer between 1 to 2497 of SEQ ID	R23797, R24081, R24137, R24753,
L	NO:100, b is an integer of 15 to 2511, where both a	R32662, R36359, R45484, R45484,

l bind		
	b correspond to the positions of nucleotide	R63380, R63433, R70942, R70995.
	lues shown in SEQ ID NO:100, and where b is	R73973, R78964, H08973, H09543.
grea	ter than or equal to a + 14.	H16712. H16713. H20846, H20896.
		R99241, H82276, H82382, H84715,
		H85367. H85516, H89615, H95047.
		H96450, H97881. N20953, N21537,
		N22201, N25769, N29477, N30442,
l i		N37087, N42334, N42354, N66424,
		N66864, N67873, N71242, N73740,
		N94555, N99903, W45394, W46993,
		W46961, W46960, W46881, W73247,
		W90778, AA026678, AA026215.
	·	AA043908, AA044414, AA042828,
	•	AA062957, AA076063, AA121145,
		AA121476, AA195131, AA234043,
		AA234044, AA426421
775844 Pref	erably excluded from the present invention are	T73286, T66741, T66742, R12147.
	or more polynucleotides comprising a nucleotide	R15080, R19321, R39271, R42973,
	ence described by the general formula of a-b,	R44589, R44589, H06197, H08725,
	re a is any integer between 1 to 2967 of SEQ ID	R94752, H71652, H71653, H79764,
	101, b is an integer of 15 to 2981, where both a	H79765, H79770, H79762, H79761,
	b correspond to the positions of nucleotide	H79771, H92246, H96184, N45199,
	lues shown in SEQ ID NO:101, and where b is	W93244, W93245, W93258, W93257,
	ter than or equal to a + 14.	W94615, W94654, AA001180,
grea	ter than or equal to a + 14.	
l '		AA039582, AA039689, AA082198,
777760	111.116	AA157370, AA157869, AA253368
	erably excluded from the present invention are	
	or more polynucleotides comprising a nucleotide	
	ence described by the general formula of a-b,	
	re a is any integer between 1 to 2790 of SEQ ID	
	102, b is an integer of 15 to 2804, where both a	
	b correspond to the positions of nucleotide	
	lues shown in SEQ ID NO:102, and where b is	
	ter than or equal to a + 14.	
	erably excluded from the present invention are	T67628, T72838, H59238, H84693,
	or more polynucleotides comprising a nucleotide	N80048, W07009, W37555, W39191,
	ence described by the general formula of a-b,	N90251, AA057629
	re a is any integer between 1 to 708 of SEQ ID	·
	103, b is an integer of 15 to 722, where both a	
	b correspond to the positions of nucleotide	
resid	lues shown in SEQ ID NO:103, and where b is	
grea	ter than or equal to a + 14.	
	erably excluded from the present invention are	T66609, T66610, T83560, R15983,
one	or more polynucleotides comprising a nucleotide	R15984, R35702, R49338, R49338,
sequ	ence described by the general formula of a-b,	H11613, R94244, H87098, H87745,
	re a is any integer between 1 to 1622 of SEQ ID	W60710, W60772, W94034,
	104, b is an integer of 15 to 1636, where both a	AA258151, AA258913, AA425943
	,	, - 100 0 10 1, 1 11 120 0 x 15 ; 1 12 12 0 x 10
NO:		
NO: and	b correspond to the positions of nucleotide	
NO: and resid	b correspond to the positions of nucleotide lues shown in SEQ ID NO: 104, and where b is	[
NO: and resid grea	b correspond to the positions of nucleotide lues shown in SEQ ID NO:104, and where b is ter than or equal to a + 14.	
NO: and resic grea 781445 Pref	b correspond to the positions of nucleotide lues shown in SEQ ID NO:104, and where b is ter than or equal to a + 14. erably excluded from the present invention are	
NO: and resic grea 781445 Pref one	b correspond to the positions of nucleotide lues shown in SEQ ID NO:104, and where b is ter than or equal to a + 14. erably excluded from the present invention are or more polynucleotides comprising a nucleotide	
NO: and resic grea 781445 Pref one sequ	b correspond to the positions of nucleotide lues shown in SEQ ID NO:104, and where b is ter than or equal to a + 14. erably excluded from the present invention are polynucleotides comprising a nucleotide ence described by the general formula of a-b,	
NO: and resic grea 781445 Pref one sequ whe	b correspond to the positions of nucleotide lues shown in SEQ ID NO:104, and where b is ter than or equal to a + 14. erably excluded from the present invention are or more polynucleotides comprising a nucleotide ence described by the general formula of a-b, re a is any integer between 1 to 1547 of SEQ ID	
NO: and resic grea 781445 Pref one sequ whe NO:	b correspond to the positions of nucleotide lues shown in SEQ ID NO:104, and where b is ter than or equal to a + 14. erably excluded from the present invention are polynucleotides comprising a nucleotide ence described by the general formula of a-b,	

	greater than or equal to a + 14.	
781531	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	1
	sequence described by the general formula of a-b.	<u> </u>
	where a is any integer between 1 to 472 of SEQ ID	
	NO:106, b is an integer of 15 to 486, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:106, and where b is	1
	greater than or equal to a + 14.	
783018	Preferably excluded from the present invention are	R18976
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
i	where a is any integer between 1 to 786 of SEQ ID	,
	NO:107, b is an integer of 15 to 800, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:107, and where b is	
	greater than or equal to $a + 14$.	
783097	Preferably excluded from the present invention are	
103071	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
		i i
	where a is any integer between 1 to 1044 of SEQ ID NO:108, b is an integer of 15 to 1058, where both a	}
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:108, and where b is	
	greater than or equal to a + 14.	
784198	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1062 of SEQ ID	
	NO:109, b is an integer of 15 to 1076, where both a	1
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:109, and where b is	<u>'</u>
	greater than or equal to a + 14.	
784868	Preferably excluded from the present invention are	1
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1185 of SEQ ID	-
	NO:110, b is an integer of 15 to 1199, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:110, and where b is	
	greater than or equal to a + 14.	
785428	Preferably excluded from the present invention are	T47751, T39348, T39359, T98137,
	one or more polynucleotides comprising a nucleotide	T79193, T95760, R16653, R16654,
	sequence described by the general formula of a-b,	R24052, R24245, R33230, R44846,
	where a is any integer between 1 to 3616 of SEQ ID	R50794, R50912, R44846, R60930,
	NO:111, b is an integer of 15 to 3630, where both a	R61049, R71116, R71620, R77888,
	and b correspond to the positions of nucleotide	R80860, H00109, H04333, H04688,
	residues shown in SEQ ID NO:111, and where b is	H05041, H09555, H30257, H30320,
	greater than or equal to a + 14.	H47931, R94218, R99062, R99260,
1	Broater man or equal to a . 17.	H50702, H50803, H52629, H52628,
		H54000, H67115, H70269, H83460,
1		H83572, H84911, H99358, N21482,
	·	N21632, N24626, N33762, N41609,
		N67949, N69593, N70188, N71452,
		N71818, N77888, N79031, N99501,
		W02150. W03072, W05781, W19647,
L		W19972, W20125, W30896, W33043

		W33197, W35407, W37262, W39072,
	· ·	W47654. W52846, W56143, W60064.
İ		W60074. W65501, W67522, W67591,
İ		
İ		W69745, W69926, W80811, W94093,
		W94156, N90996, AA039462,
		AA040857, AA043084, AA043810,
		AA053423, AA053042, AA064625,
1		AA064709, AA115540, AA115051,
1		AA120833. AA129500. AA129499,
ļ		AA146736. AA148602, AA152314,
		AA150343. AA150620, AA150790,
1-		AA157282, AA160296, AA173937,
		AA173969, AA181340, AA188207,
		AA186354, AA188646, AA190484,
		AA199676, AA199677, AA243342,
l		AA250981, AA459647, AA459773,
		AA460227
785845	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1512 of SEQ ID	
	NO:112, b is an integer of 15 to 1526, where both a	
1	and b correspond to the positions of nucleotide	
ľ	residues shown in SEQ ID NO:112, and where b is	ļ ·
705054	greater than or equal to a + 14.	TO COOL 11/45204
785854	Preferably excluded from the present invention are	T85881, W45204
	one or more polynucleotides comprising a nucleotide	1
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 571 of SEQ ID	
	NO:113, b is an integer of 15 to 585, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:113, and where b is	
	greater than or equal to a + 14.	
786705	Preferably excluded from the present invention are	R09422
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 487 of SEQ ID	
	NO:114, b is an integer of 15 to 501, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:114, and where b is	
	greater than or equal to a + 14.	· ·
787186	Preferably excluded from the present invention are	
. 57 100	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 1951 of SEQ ID	
	NO:115, b is an integer of 15 to 1965, where both a	
	and b correspond to the positions of nucleotide	· I
	residues shown in SEQ ID NO:115, and where b is	
	greater than or equal to a + 14.	
787279	Preferably excluded from the present invention are	T62081, T97170, R17585, R42923,
	one or more polynucleotides comprising a nucleotide	R48789, R48896, R54561, R54562,
	sequence described by the general formula of a-b,	R54721, R54722, R42923, R72984,
		R73595, H23901, H43508, H46275,
		H46348, H47255, H47254, R83475,
		R89352, R91048, R93150, R93669,
	residues shown in SEQ ID NO:116, and where b is	R94520, R98839, H48417, H48899,
	greater than or equal to a + 14.	H48900, H50560, H54157, H58936,
	Brono. man or oquar to a . 17.	F, 1134137, 1136730,

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		H58983, H67630, H69455, H72554.
1		H72955, H89822, N23388, N33070.
1		N35168. N40256. N44641. N52556.
		N59706, N68387, N80806, N92514,
		W17007, W19578, W20217, W38835.
1		W49822, W56061. W65416, W65285.
1		
		N90575, AA002190, AA045344,
		AA045446, AA052950, AA053432,
		AA082245, AA083753, AA102071,
		AA099961, AA101574, AA112070,
}		AA125782, AA125931, AA135139.
		AA135268, AA146635, AA151603,
İ		AA149484, AA149981, AA152120,
1		AA171975, AA172123, AA181805,
ļ		AA181821, AA188148, AA188225,
1		AA186556, AA186917, AA460297,
		AA461585
789002	Preferably excluded from the present invention are	
j	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
-	where a is any integer between 1 to 695 of SEQ ID	•
	NO:117, b is an integer of 15 to 709, where both a	
· ·	and b correspond to the positions of nucleotide	
.	residues shown in SEQ ID NO:117, and where b is	
	greater than or equal to a + 14.	
789008	Preferably excluded from the present invention are	T47492, T47493, T47900, T48303,
i	one or more polynucleotides comprising a nucleotide	T48445, T48456, T49007, T49079,
ļ	sequence described by the general formula of a-b,	T49080, T49218, T49310, T49311,
ŀ	where a is any integer between 1 to 2039 of SEQ ID	T49913, T49914, T49941, T51256,
	NO:118, b is an integer of 15 to 2053, where both a	T51337, T51371, T51423, T51604,
1	and b correspond to the positions of nucleotide	T51757, T52271, T52400, T53326,
	residues shown in SEQ ID NO:118, and where b is	T53327, T54148, T54244, T54295,
	greater than or equal to a + 14.	T54330, T54402, T54407, T55485,
	F	T55733, T56237, T56379, T56414,
		T56565, T39384, T40546, T40551,
ĺ		T40552, T40824, T89603, T79470,
	·	T79561, R01378, R12635, R20536,
		R21209, R21238, R21239, R22062,
		R22119, R22190, R22241, R22534,
		R22535, R22823, R23625, R23881,
		R24090, R25741, R26431, R26587,
		R28327, R28328, R28330, R31619,
1	,	
		R32132, R32349, R33134, R33286,
		R35454, R36658, R39739, R50498,
		R50581, R20536, R56656, R65717,
		R65777, R65870, R67856, R67857,
		R68076, R69399, R69531, R69752,
		R69920, R71289, R72350, R74061,
]		R77148, R77149, R80495, R80640,
		R82550, H00862, H01301, H01472,
		H01571, H02637, H02893, H03072,
		H03073, H03443, H03525, H03812,
		H03836, H23457, H23458, H26513.
		H26583, H26584, R86226, R86227,
•		R87053, R91130, R91174, R92513.
		R92642, R93418, R93468, R93700.
	1	R94462, R94463, R94793, R95110,

		R96330. R96329, R96675, R96943,
		R97000, R98195, R99857, H48277,
		H48366, H48451, H53119, H54247,
1		H54246, H57144, H57217, H58791,
		H59276, H59324, H59614, H59654.
1		H62873, H62997, H66302, H67109,
1		H67468, H67594, H67634, H67646,
1		H67685, H67891, H67935, H68007,
1		H68476, H72996, H73208, H73882,
		H74057, H74076, H74196, H75522,
ł		H75366, H77704, H77705, H78593,
1		H79262. H79373, H81287, H81343,
1	·	H82036, H82218, H82313, H87010,
	·	H87011, H90552, H90551, H93198,
1		H94403, N28269, N30773, N34862,
		N38975, N38989, N39317, N43935,
	1	N45164, N48122, N48136, N50666,
1		N50756, N52570, N53559, N53589,
	 	N55006, N55026. N57654, N58258,
1		N58340, N58627, N58738, N70218,
		N72552, N72649, N77216, N77511,
		N77635. N80637, W01074, W58701,
		W68231, W68232, W68700, W72561,
1		W72580, W72399, W76223, W85725,
	<u> </u>	W92304, W92318, W92144, W92354,
		AA004478, AA004551, AA009715,
		AA009825, AA024464, AA024465,
		AA025660, AA039523, AA039522,
		AA040081, AA040128, AA040033,
	· ·	AA040827, AA045744, AA053323,
		AA099152, AA099250
789555	Preferably excluded from the present invention are	T85669, H62189, H62190, H73963,
	one or more polynucleotides comprising a nucleotide	H73295, N74147, W04314, W23625,
	sequence described by the general formula of a-b,	W35215, AA040573, AA040671
	where a is any integer between 1 to 1810 of SEQ ID	
	NO:119, b is an integer of 15 to 1824, where both a	
ł	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:119, and where b is	
	greater than or equal to a + 14.	
789631	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 592 of SEQ ID	
	NO:120, b is an integer of 15 to 606, where both a	į
	and b correspond to the positions of nucleotide]
	residues shown in SEQ ID NO:120, and where b is	
	greater than or equal to a + 14.	·
789779	Preferably excluded from the present invention are	N69694, AA151932
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 824 of SEQ ID	
	NO:121, b is an integer of 15 to 838, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:121, and where b is	
	greater than or equal to a + 14.	
790387		H19654, H87102, H87749, N29354,
		N34298, N44187, N57052, W69612,
	The part of the pa	, 111107, 1117032, W09012,

Γ	company described by the convert formula of a h	W02044 W02065 A 4 027002
	sequence described by the general formula of a-b.	W93844, W93865, AA027893.
	where a is any integer between 1 to 642 of SEQ ID NO: 122, b is an integer of 15 to 656, where both a	AA029638, AA058317, AA058495,
	and b correspond to the positions of nucleotide	AA179870. AA232827. AA233881, AA235809
	residues shown in SEQ ID NO:122, and where b is	MA233809
	greater than or equal to a + 14.	
790461	Preferably excluded from the present invention are	R66275, R76171, R82537, AA054476,
, , , , , , , , , , , , , , , , , , ,		
	sequence described by the general formula of a-b,	AA151006, AA150976
	where a is any integer between 1 to 1372 of SEQ ID	AA131000, AA130970
	NO:123, b is an integer of 15 to 1386, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:123, and where b is	
	greater than or equal to a + 14.	
790931	Preferably excluded from the present invention are	T92052, R10686, T84927, R21818,
7,0751	one or more polynucleotides comprising a nucleotide	R22331, R22332, R22401, R23139,
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 831 of SEQ ID	R23140, R23369, R32153, R32154,
	NO:124, b is an integer of 15 to 845, where both a	R63527, R63575, R68799, R68901,
	and b correspond to the positions of nucleotide	R80768, H12779, H12836, H56522, H56704, H94832, H96055, H96058,
	residues shown in SEQ ID NO:124, and where b is	
	greater than or equal to a + 14.	H96422, H96418, N26715, N27088, N31910, N32532, N33383, N34596,
	greater than or equal to a + 14.	N42693, N42748, W32121, W37432,
		W44577, W44627, W51792, W61294,
791176	Preferably excluded from the present invention are	W65390, AA026773, AA026774 T51708, T51919, T69384, R50942,
//11/0	one or more polynucleotides comprising a nucleotide	R73632, R73706, H28125, N22822,
	sequence described by the general formula of a-b,	N78772
	where a is any integer between 1 to 1642 of SEQ ID	14/6//2
	NO:125, b is an integer of 15 to 1656, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:125, and where b is	
	greater than or equal to a + 14.	
791983	Preferably excluded from the present invention are	
,,,,,,,	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 823 of SEQ ID	
	NO:126, b is an integer of 15 to 837, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:126, and where b is	
	greater than or equal to a + 14.	
792539	Preferably excluded from the present invention are	H53623, H53662, N23079, N69293,
	one or more polynucleotides comprising a nucleotide	N89689, AA034518, AA035409,
	sequence described by the general formula of a-b,	AA035410, AA046490, AA046762,
	where a is any integer between 1 to 1203 of SEQ ID	AA085037, AA085105, AA134976,
	NO:127, b is an integer of 15 to 1217, where both a	AA135078, AA459951, AA460040
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:127, and where b is	
792749	greater than or equal to a + 14	4
792749	greater than or equal to a + 14. Preferably excluded from the present invention are	R13058 R13951 R40011 P51765
792749	Preferably excluded from the present invention are	R13058, R13951, R40011, R51765, R51766, R40011, R67629, R67630
792749	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	R51766, R40011, R67629, R67630,
792749	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	R51766, R40011, R67629, R67630, H01808, H29310, H29403, R99196,
792749	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1335 of SEQ ID	R51766, R40011, R67629, R67630, H01808, H29310, H29403, R99196, H52742, H52788, H61636, H71767,
792749	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1335 of SEQ ID NO:128, b is an integer of 15 to 1349, where both a	R51766, R40011, R67629, R67630, H01808, H29310, H29403, R99196, H52742, H52788, H61636, H71767, H71768, N20919, N27779, N36030,
792749	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1335 of SEQ ID NO:128, b is an integer of 15 to 1349, where both a	R51766, R40011, R67629, R67630, H01808, H29310, H29403, R99196, H52742, H52788, H61636, H71767,

		W57869. W58140, W86456, N90422, AA029174. AA029253, AA031374. AA031375. AA062913, AA082549, AA133965. AA167773. AA166872, AA176295. AA176395, AA428235
792961	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2304 of SEQ ID NO:129, b is an integer of 15 to 2318, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.	
793206	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b. where a is any integer between 1 to 2135 of SEQ ID NO:130, b is an integer of 15 to 2149, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to a + 14.	
793249	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1006 of SEQ ID NO:131, b is an integer of 15 to 1020, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.	T48358, T48359, T71001, T71063, T72193, T72972, T67531, T69528, T86709, T86804, T89854, T90890, T91159, T85694, T85895, T95466, T95467, R00007, R00008, R12353, R23932, R23933, R37279, R63973, R64080, R73825, R73826, R76905, R77073, R77445, R77538, R79797, R79808, R79894, R79908, H11925, H11926, H15192, H16754, H16862, H19737, H20072, H21725, H22675, H24523, H26125, H26391, H39766, H41271, H41373, H41374, H43544, H43545, H44881, H45180, H45181, R92671, R94833, H57801, H58122, H58123, H62248, H62337, H69587, H69586, H80840, H80930, H85462, H85747, H86829, H86902, H96591, H96708, H97829, H99614, N25266, N26147, N27161, N29792, N33452, N33767, N33906, N36535, N38816, N39177, N40101, N42935, N42425, N44530, N45252, N45445, N57801, N59012, N78685, N79046, N91819, N98480, W02726, W04566, W15191, W15596, W17335, W24253, W25723, W30937, W31253, W31429, W31674, W39685, W44989, W46619, W46654, W57768, W57804, W57841, W57622, W67135, W67136, W73878, W73364, W73441, W77815, W80810, W80903, W92682, W92512, W92513, W96375, W96526, AA001447, AA001482, AA021374, AA021375, AA037268, AA037489, AA037569, AA039708, AA040262, AA040417, AA057011,

		1
		AA074646, AA074679, AA075303,
[AA088467, AA098947, AA100987,
]		AA126026, AA126122, AA126778,
ļ		AA128010, AA128034, AA136619,
ļ		AA136750, AA143234, AA143291,
ļ		AA143564, AA143565, AA146915,
1		AA151446, AA151447, AA156218,
ł		AA157383, AA159151, AA173294,
		AA179768, AA180442, AA181155,
		AA181156, AA181722, AA186611,
1		AA188254, AA190686, AA191758,
[AA191547, AA195441, AA223540,
1		AA223587
793626	Preferably excluded from the present invention are	71722350
1,,,,,,	one or more polynucleotides comprising a nucleotide	•
Į.	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 2305 of SEQ ID	ļ .
Ī		
	NO:132, b is an integer of 15 to 2319, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:132, and where b is	
704417	greater than or equal to a + 14.	
794417	Preferably excluded from the present invention are	
Ī	one or more polynucleotides comprising a nucleotide	
ĺ	sequence described by the general formula of a-b,	
l	where a is any integer between 1 to 1359 of SEQ ID	
l	NO:133, b is an integer of 15 to 1373, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:133, and where b is	
L	greater than or equal to a + 14.	
795197	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
ŀ	where a is any integer between 1 to 1643 of SEQ ID	
	NO:134, b is an integer of 15 to 1657, where both a	
ļ	and b correspond to the positions of nucleotide	
ľ	residues shown in SEQ ID NO:134, and where b is	
	greater than or equal to a + 14.	·
795251	Preferably excluded from the present invention are	T89826, T74514, T89080, R24028,
		H03686, H97493, N54611, W94797,
	sequence described by the general formula of a-b,	W94798, AA129537, AA190765,
	1	AA191357, AA256363, AA425151,
	NO:135, b is an integer of 15 to 2360, where both a	AA429405
i	and b correspond to the positions of nucleotide	AA427403
	residues shown in SEQ ID NO:135, and where b is	
705752	greater than or equal to a + 14.	
795752	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 1028 of SEQ ID	
	NO:136, b is an integer of 15 to 1042, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:136, and where b is	
	greater than or equal to a + 14.	
796261	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1023 of SEQ ID	
	1	

		· · · · · · · · · · · · · · · · · · ·
	NO:137. b is an integer of 15 to 1037, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:137, and where b is	
	greater than or equal to a + 14.	
796933	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1476 of SEQ ID	
	NO:138. b is an integer of 15 to 1490, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:138, and where b is	
	greater than or equal to a + 14.	•
799424	Preferably excluded from the present invention are	
77727	one or more polynucleotides comprising a nucleotide	
i	sequence described by the general formula of a-b,	
]	where a is any integer between 1 to 1670 of SEQ ID	
1	NO:139, b is an integer of 15 to 1684, where both a	
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:139, and where b is	
1	· ·	
700600	greater than or equal to a + 14.	
799698	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 413 of SEQ ID	
	NO:140, b is an integer of 15 to 427, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:140, and where b is	
	greater than or equal to a + 14.	
800351	Preferably excluded from the present invention are	
]	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 875 of SEQ ID	
	NO:141, b is an integer of 15 to 889, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:141, and where b is	
	greater than or equal to a + 14.	
800573	Preferably excluded from the present invention are	
Ì	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1491 of SEQ ID	
	NO:142, b is an integer of 15 to 1505, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:142, and where b is	
	greater than or equal to a + 14.	
805815	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1221 of SEQ ID	
:	NO:143, b is an integer of 15 to 1235, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:143, and where b is	
	greater than or equal to a + 14.	
906445	_ 	
806445	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1406 of SEQ ID	
	NO:144, b is an integer of 15 to 1420, where both a	

	and b correspond to the positions of nucleotide	
ļ	residues shown in SEQ ID NO:144, and where b is	
	greater than or equal to a + 14.	
810309	Preferably excluded from the present invention are	,
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	•
	where a is any integer between 1 to 1905 of SEQ ID	
	NO:145. b is an integer of 15 to 1919, where both a	
]	and b correspond to the positions of nucleotide	ļ.
	residues shown in SEQ ID NO:145, and where b is	
	greater than or equal to a + 14.	
811022	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 1365 of SEQ ID]
1	NO:146, b is an integer of 15 to 1379, where both a	i
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:146, and where b is	İ
1		
811023	greater than or equal to a + 14. Preferably excluded from the present invention are	
011025	one or more polynucleotides comprising a nucleotide	
ĺ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 500 of SEQ ID	1
		1
	NO:147, b is an integer of 15 to 514, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:147, and where b is	
211142	greater than or equal to a + 14.	
811143	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2044 of SEQ ID	
	NO:148, b is an integer of 15 to 2058, where both a	
	and b correspond to the positions of nucleotide	
-	residues shown in SEQ ID NO:148, and where b is	
	greater than or equal to a + 14.	
811381	Preferably excluded from the present invention are	·
ļ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1767 of SEQ ID	
	NO:149, b is an integer of 15 to 1781, where both a	
ı	and b correspond to the positions of nucleotide	<u> </u>
ı	residues shown in SEQ ID NO:149, and where b is	
	greater than or equal to a + 14.	
811595	Preferably excluded from the present invention are	T51013, T51104, T54094, T54185,
	one or more polynucleotides comprising a nucleotide	T68577, T68655. T90261, T90702,
	sequence described by the general formula of a-b,	T92691, R34639, R49168, R51392,
	where a is any integer between 1 to 1695 of SEQ ID	R49168, R84952, R84994, H84723,
	NO:150, b is an integer of 15 to 1709, where both a	H84890, N29820, N42512, N64677,
	and b correspond to the positions of nucleotide	N67206, N73458, N80110, N92710,
	residues shown in SEQ ID NO:150, and where b is	W02861, W20327, W23680, W76675,
	greater than or equal to a + 14.	AA031294, AA062736, AA062781,
	Diversity of Odder to a 1 14.	AA070243, AA070244, AA084464,
	•	14 4 100714 A 4 100767 A 4 126726
	1	AA100714, AA100767, AA136726,
		AA136684, AA191613, AA223541, AA223589, AA252636
813000	Preferably excluded from the present invention are	MACCO 2007, MACO 2000
113000	one or more polynucleotides comprising a nucleotide	
		T

	sequence described by the general formula of a-b,	1
	where a is any integer between 1 to 908 of SEQ ID	1
	NO:151, b is an integer of 15 to 922, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:151, and where b is	
	greater than or equal to a + 14.	
813288	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 621 of SEQ ID	
l	NO:152, b is an integer of 15 to 635, where both a	
	and b correspond to the positions of nucleotide	
ì	residues shown in SEQ ID NO:152, and where b is	
	greater than or equal to a + 14.	
813431	Preferably excluded from the present invention are	T94237, T89464, T89552, R09285,
	one or more polynucleotides comprising a nucleotide	T78198, R14453, R15241, R15311,
ļ	sequence described by the general formula of a-b,	R21130, R33140, R33292, R40972,
	where a is any integer between 1 to 2314 of SEQ ID	R46726, R42211, R40972, R46726,
	NO:153, b is an integer of 15 to 2328, where both a	R66207, R67085, R73679, R73770,
1	and b correspond to the positions of nucleotide	H12485, H19135, H22930, H24111,
	residues shown in SEQ ID NO:153, and where b is	H26774, H26884, R89854, R89894.
j	greater than or equal to a + 14.	R92012, R92057, H53798, H61991,
		H61992, H64854, H65452, H73213,
		H74063, H79753, H79754, H80620.
		H80654, H81209, H81210, H84019.
		H84020, N35581, N68664, N73792,
		N91681, N92730, N99417, W20349,
1		W46901, W52684, W60422, W61136,
ļ		W61108, W61174, W68119, W73989,
		W79021, W79231, W80414, W80777,
{		W80930, AA040315, AA045023,
		AA045024, AA045188, AA045352,
		AA181735, AA181799, AA223229,
		AA223428, AA464186, AA464780,
		AA428152, AA430305
813450	Preferably excluded from the present invention are	Г90954, Т84401, Т85262, R22109,
015450		R48652, R72000, R73453, H14261,
	1	
		H27403, H42017, H42018, H38149,
	1	H38150, H69302, H69397, N98775,
	1	AA148803, AA150212
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:154, and where b is	
1		
813478	greater than or equal to a + 14.	
0174/0	Preferably excluded from the present invention are	
!	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 4285 of SEQ ID	
	NO:155, b is an integer of 15 to 4299, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:155, and where b is	
	greater than or equal to a + 14.	
813505	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	• • • • • • • • • • • • • • • • • • • •	
	where a is any integer between 1 to 992 of SEQ ID	
	where a is any integer between 1 to 992 of SEQ ID NO:156, b is an integer of 15 to 1006, where both a	

Rester than or equal to a + 14.			r
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1672 of SEQ ID NO:157, b is an integer of 15 to 1686, where both a nand b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14. 15606	l	residues shown in SEQ ID NO:156, and where b is	
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1672 of SEQ ID NO:157, b is an integer of 15 to 1686, where both a nand b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14. 815606 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4133 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one	016653		
sequence described by the general formula of a-b, where a is any integer between 1 to 1672 of SEQ ID NC:157, b is an integer of 15 to 1686, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14. 815606 Preferably excluded from the present invention are or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 413 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1238 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in S	813332		
where a is any integer between 1 to 1672 of SEQ ID NO:157, b is an integer of 15 to 1686, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14. 815606 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1413 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. 815606 Signature of 15 to 1417, where both a not be correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. 815606 Signature of 15 to 1417, where both a not sequence described by the general formula of a-b, where a is any integer between 1 to 128 of SEQ ID NO:159, b is an integer of 15 to 1247, where both a not or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a not or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in			•
NO: 157, b is an integer of 15 to 1686, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 157, and where b is greater than or equal to a + 14. 815606 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4133 of SEQ ID NO: 158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 158, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide polynucleotide residues shown in SEQ ID NO: 159, and 169647, AA169322, AA187099, AA099478, AA099478, AA169057, AA15914, AA224513, AA224493, AA15914, AA224513, AA224493, AA15914, AA224513, AA224513, AA224514, AA224513, AA224513, AA224514, AA224513, AA224513, AA224593, AA224514, AA224593, AA255944, AA2392144, AA2356948, AA256944, AA29442 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO: 159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO: 159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 10 to 128 of SEQ ID NO: 159, and wher			
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14. 815606 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4133 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1247, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816048 Preferably excluded from the present invention are one or more polynucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. 816			
Residues shown in SEQ ID NO: 157, and where b is greater than or equal to a + 14.			
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 413 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. 14			
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4133 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID No:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one of more polynucleotides of the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides of the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a			
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4133 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. N50022, N51861, N54126, N54677, W16972, W32896, W35293, W38598 N89624, N90277, AA027830, AA07892, AA078891, AA099437, AA099478, AA101431, AA112543, AA121794, AA129629, AA136231, AA143110, AA150576, AA157125, AA158242, AA158709, AA15976, AA160357, AA160437, AA169622, AA173082, AA18709, AA224150, AA227518, AA225414, AA2224513, AA222458, AA225718, AA2254514, AA2224513, AA222488, AA225794, AA27396, AA27518, AA27518, AA27548, AA27549442 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, which is a proper of the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present inventi	015606		T(0162 T(0212 T00000 T00227
sequence described by the general formula of a -b, where a is any integer between 1 to 4133 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a nd b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. No:022, N51861, N54126, N54677, N5062, A078892, A035739, A05886, A069223, A078893, A078896, A078891, A099437, A099478, AA101431, AA112543, AA121794, AA129629, AA136251, AA143104, A160576, AA157125, AA158242, AA158709, AA159976, AA166947, AA169822, AA137802, AA166647, AA169822, AA178709, AA224514, AA224513, AA224488, AA26779, AA227360, AA227430, AA2274314, AA224513, AA224488, AA25779, AA227364, AA227488, AA255494, AA229442 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Stock	812606		
where a is any integer between 1 to 4133 of SEQ ID NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. **N50022, N51861, N54126, N54678, N59624, N90277, AA027830, AA078890, AA078891, AA069223, AA078890, AA078891, AA069223, AA078890, AA078891, AA069223, AA078890, AA078891, AA069223, AA163251, AA143110, AA150576, AA165712, AA168242, AA158709, AA1659976, AA160357, AA159941, AA169976, AA160357, AA159491, AA169976, AA160357, AA159491, AA16947, AA169822, AA173082, AA187009, AA224150, AA224303, AA224514, AA224513, AA224513, AA224513, AA224513, AA224514, AA223799, AA227518, AA232104, AA232580, AA256938, AA256944, AA429442 **S16048** **Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. **S16048** **Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. **R49817**, H29904**, H39626, H39718**, H29904**, H39626, H39718**, H49715**, H42210**, H42281**, H42354**, H42710**, H43124**, R83615**, R86066, R92103, R92104**, R96726**, R96727**, H39738**, H39881**, H40715**, H42210**, H42281**, H42354**, H42710**, H43124**, R83615**, R86066, R92103, R99104**, R96726**, R96727**, R95726**, R95298**, R95959**, R95655**, N87655**, N89960**, AA075720**, AA045521**, AA045720**, AA045720**, AA045720**, AA045720**, AA045720**, AA045720**, AA045720**, AA045			
NO:158, b is an integer of 15 to 4147, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. N50022, N51861, N54126, N54677, W16972, W32896, W35293, W38598 N89624, N90277, AA027830, AA027892, AA035739, AA025806, AA0679223, AA078599, AA078891, AA099437, AA099478, AA101431, AA112543, AA121794, AA129629, AA15976, AA165151, AA164643, AA166799, AA159976, AA160357, AA1659491, AA169647, AA169822, AA173082, AA169647, AA169822, AA173082, AA169647, AA169822, AA173082, AA169647, AA169822, AA173082, AA224514, AA2224510, AA224303, AA224514, AA224513, AA2244518, AA223580, AA255948, AA225694, AA429442 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R1907, R1948, R272113, R29818, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83115, R80666, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62233, H62342, H80441, H89111, H97591, H99947, N27565, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA007903, AA027132, AA045720, AA045022, AA045721, AA045721, AA045720, AA045021, AA045021, AA045021, AA045021, AA045021, AA045021, AA045021, AA045021, AA045021, AA045021, AA045081, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA083394, AA085101, AA074787, AA0835101, AA074787, AA0835101, AA074787, AA083510	ţ		
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. Noso22, NS1861, NS4126, NS4677, W16972, W32896, W35293, W38598 N38624, N90277, AA027830, AA027892, AA035739, AA055806, AA069223, AA078890, AA078891, AA099437, AA099478, AA101431, AA112543, AA121794, AA129629, AA136251, AA143110, AA15076, AA1571125, AA158242, AA158709, AA1606374, AA160629, AA165150, AA165151, AA164643, AA166029, AA165150, AA165151, AA164643, AA166029, AA165150, AA224184, AA224303, AA224514, AA224315, AA224303, AA224514, AA224315, AA224303, AA224514, AA224514, AA224315, AA225494, AA29442 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29811, H29917, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86666, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027872, AA045502, AA045211, AA045720, AA045201, AA045820, AA058204, AA074787, AA082394, AA085101, AA074787, AA082394, AA085101, AA074787, AA082394, AA085101, AA074787, AA082394, AA085101, AA074787, AA082394, AA085101, AA074787	1		_ · · · · · · · · · · · · · · · · · · ·
residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14. W16972, W32896, W35293, W38598 W39624, N90277, AA027830, AA027882, AA035739, AA055806, AA069223, AA078890, AA078891, AA099437, AA099437, AA109431, AA112543, AA121794, AA129629, AA136251, AA143110, AA150576, AA157125, AA158242, AA158709, AA159976, AA160629, AA165150, AA165151, AA160634, AA160629, AA1665150, AA165151, AA160647, AA160629, AA166799, AA187009, AA224130, AA224313, AA224314, AA224514, AA224513, AA224488, AA226779, AA227396, AA227396, AA227396, AA227396, AA227396, AA227396, AA225494, AA429442 B16048			
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AA069223. AA078890. AA078891. AA099437, AA121794, AA129629. AA136251, AA143110. AA150576. AA157125, AA158242, AA158709. AA15976. AA160357. AA160357. AA1659491. AA160534. AA160629. AA165150. AA165151, AA164643, AA166799. AA169647. AA169822. AA173082. AA187009. AA224150. AA224303. AA224514, AA224513, AA224488. AA226779. AA227396. AA227318. AA232104, AA232580, AA256938. AA255494. AA429442 Freferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907. R71948, R72113, R72818, r93566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA045721, AA045720, AA046280, AA05824, AA074786, AA074787, AA082394, AA085101,	1	greater than or equal to a + 14.	
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AA187009, AA224150, AA224303, AA224514, AA224513, AA224488, AA226779, AA227396, AA227518, AA232104, AA232580, AA256938, AA255494, AA429442 B16048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R19907, R71948, R72113, R72818, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045721, AA045720, AA046287, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			1
AA224514, AA224513, AA224488, AA226779, AA227396, AA227518, AA232104, AA2322580, AA256938, AA255494, AA429442 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045721, AA045720, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	İ		1
AA226779, AA227396, AA227518, AA232104, AA232580, AA256938, AA255494, AA429442 B16048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. B16048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. B16048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide R48419, R48536, R48532, R48658, R48658, R48658, R48658, R48658, R49781, R488511, R593210, R66870, R67958, R69435, R69517, R70414, R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA045022, AA045721, AA045720, AA045021, AA045721, AA045720, AA045021, AA045721, AA045720, AA045011, AA045720, AA045824, AA074787, AA082394, AA085101,	i		
A232104, AA232580, AA256938, AA255494, AA429442 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			1
B16048 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045221, AA045222, AA045721, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide R48419, R48536, R48537, R48569, R48582, R48668, R48683, R49781, R49827, R53111, R53210, R66870, R67958, R69435, R69517, R70414, R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R48582, R48668, R48683, R49781, R49827, R53111, R53210, R66870, R67958, R69435, R69517, R70414, R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045220, AA045721, AA045247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	816048		· · · · · · · · · · · · · · · · · · ·
where a is any integer between 1 to 1228 of SEQ ID NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R49827, R53111, R53210, R66870, R67958, R69435, R69517, R70414, R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	ŀ		
NO:159, b is an integer of 15 to 1242, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R67958, R69435, R69517, R70414, R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	İ		
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R71907, R71948, R72113, R72818, R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	·		
residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14. R73269, R75924, R75959, R79565, R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	ŀ		1
greater than or equal to a + 14. R79566, R80393, H25645, H26211, H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	ļ		
H29817, H29904, H39626, H39738, H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	ŀ		R73269, R75924, R75959, R79565,
H39881, H40715, H42210, H42281, H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	ļ	greater than or equal to a + 14.	
H42354, H42710, H43124, R83615, R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	İ		H29817, H29904, H39626, H39738,
R86066, R92103, R92104, R96726, R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
R96727, H54075, H54232, H54233, H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247. AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
H62253, H62342, H80441, H80442, H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			R86066, R92103, R92104, R96726,
H91114, H97541, H99927, N27357, N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247. AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,	ļ		R96727, H54075, H54232, H54233,
N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247. AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			H62253, H62342, H80441, H80442,
N27665, N93636, W19226, W19703, W25418, W25514, W44404, W63554 W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247. AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			H91114, H97541, H99927, N27357,
W78078, N89960, AA027093, AA027132, AA045021, AA045022, AA045721, AA045720, AA046247. AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			N27665, N93636, W19226, W19703,
AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			W25418, W25514, W44404, W63554,
AA027132, AA045021, AA045022, AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
AA045721, AA045720, AA046247, AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
AA046280, AA058624, AA074786, AA074787, AA082394, AA085101,			
AA074787, AA082394, AA085101,			
AA085282, AA100996, AA127562			AA074787, AA082394, AA085101.
[AA085282, AA100996, AA127562,
AA127729, AA127784, AA128372,		_ `	AA127729, AA127784, AA128372.

one or m	ly excluded from the present invention are	AA134954, AA143611, AA148145, AA150570, AA161257, AA182028, AA188387, AA232423, AA464270, AA464381, AA421219, AA425804, AA428372
one or m	ly excluded from the present invention are	AA188387, AA232423, AA464270, AA464381, AA421219, AA425804, AA428372
one or m	ly excluded from the present invention are	AA464381, AA421219, AA425804, AA428372
one or m	ly excluded from the present invention are	AA428372
one or m	ly excluded from the present invention are	
one or m	ly excluded from the present invention are	
	ry excitated from the present invention are	R28400, R82355, R82411, H01338,
1	ore polynucleotides comprising a nucleotide	H01388, N24952, N33829, AA043471,
sequence	e described by the general formula of a-b,	AA043472, AA125807, AA128280,
where a	is any integer between 1 to 2215 of SEQ ID	AA129405, AA133871, AA129367,
NO:160,	b is an integer of 15 to 2229, where both a	AA133179, AA133312, AA131385,
and b co	rrespond to the positions of nucleotide	AA428408
	shown in SEQ ID NO:160, and where b is	
	han or equal to a + 14.	
	ly excluded from the present invention are	
	ore polynucleotides comprising a nucleotide	
	described by the general formula of a-b,	
	is any integer between 1 to 1906 of SEQ ID	
	b is an integer of 15 to 1920, where both a	
	rrespond to the positions of nucleotide	
	shown in SEQ ID NO:161, and where b is	
	nan or equal to a + 14.	1
	ly excluded from the present invention are	
	ore polynucleotides comprising a nucleotide	
	described by the general formula of a-b,	
	is any integer between 1 to 2605 of SEQ ID	
	b is an integer of 15 to 2619, where both a	
	rrespond to the positions of nucleotide	İ
	shown in SEQ ID NO:162, and where b is	
	nan or equal to a + 14.	D21022 1/20722 1/2072 1 107721
		R21933, H39733, N69879, AA027031,
	ore polynucleotides comprising a nucleotide	AA100964, AA157234, AA173338
	described by the general formula of a-b,	
	s any integer between 1 to 1405 of SEQ ID	
	b is an integer of 15 to 1419, where both a	1
	respond to the positions of nucleotide	
	shown in SEQ ID NO:163, and where b is	
	nan or equal to a + 14.	
	y excluded from the present invention are	
	ore polynucleotides comprising a nucleotide	· · · · · · · · · · · · · · · · · · ·
	described by the general formula of a-b,	
	s any integer between 1 to 3796 of SEQ ID	
	b is an integer of 15 to 3810, where both a	
	Tespond to the positions of nucleotide	
	shown in SEQ ID NO:164, and where b is	+
	ian or equal to a + 14.	
825279 Preferabl	y excluded from the present invention are	R06729, R61520, R86829, H51131,
one or me	ore polynucleotides comprising a nucleotide	N57993, W93696, AA423827
	described by the general formula of a-b,	
1 -	s any integer between 1 to 803 of SEQ ID	
	b is an integer of 15 to 817, where both a	·
	respond to the positions of nucleotide	
		T .
and b cor		
and b cor residues s	shown in SEQ ID NO:165, and where b is	
and b cor residues s greater th	shown in SEQ ID NO:165, and where b is an or equal to a + 14.	
and b cor residues s greater th 825442 Preferabl	shown in SEQ ID NO:165, and where b is that or equal to a + 14. y excluded from the present invention are	
and b cor residues s greater th Preferabl one or mo	shown in SEQ ID NO:165, and where b is an or equal to a + 14.	

1	NO:166, b is an integer of 15 to 1578, where both a	
ļ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:166, and where b is	
	greater than or equal to a + 14.	
825548	Preferably excluded from the present invention are]
ļ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	1
1	where a is any integer between 1 to 1680 of SEQ ID	1
	NO:167, b is an integer of 15 to 1694, where both a	i .
	and b correspond to the positions of nucleotide]
ł	residues shown in SEQ ID NO:167, and where b is	
	greater than or equal to a + 14.	
825725	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
i	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1622 of SEQ ID	
	NO:168, b is an integer of 15 to 1636, where both a	į
	and b correspond to the positions of nucleotide	
l .	residues shown in SEQ ID NO:168, and where b is	
	greater than or equal to a + 14.	
826639	Preferably excluded from the present invention are	
020033	one or more polynucleotides comprising a nucleotide	
l	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 653 of SEQ ID	
j	NO:169, b is an integer of 15 to 667, where both a	
l	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:169, and where b is	
	1	
827079	greater than or equal to a + 14.	
82/0/9	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3584 of SEQ ID	
	NO:170, b is an integer of 15 to 3598, where both a	
	and b correspond to the positions of nucleotide	
ļ	residues shown in SEQ ID NO:170, and where b is	
L	greater than or equal to a + 14.	·
827153	Preferably excluded from the present invention are	
<u> </u>	one or more polynucleotides comprising a nucleotide	
Ì	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 926 of SEQ ID	·
	NO:171, b is an integer of 15 to 940, where both a	
l	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:171, and where b is	
	greater than or equal to a + 14.	
827351	Preferably excluded from the present invention are	R14710, H92769, H92882, AA195498,
	one or more polynucleotides comprising a nucleotide	AA242878, AA242884, AA252152,
i	sequence described by the general formula of a-b,	AA251967, AA465181, AA465542,
	where a is any integer between 1 to 1444 of SEQ ID	AA481105, AA481210, AA492206,
	NO:172, b is an integer of 15 to 1458, where both a	AA732326
	and b correspond to the positions of nucleotide	
l	residues shown in SEQ ID NO:172, and where b is	
	greater than or equal to a + 14.	
827503	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2695 of SEQ ID	
	NO:173, b is an integer of 15 to 2709, where both a	
	p. c , o to an integer of 15 to 2707, whole both a	<u> </u>

	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:173, and where b is	
	greater than or equal to a + 14.	
827563	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
İ	where a is any integer between I to 999 of SEQ ID	
	NO:174, b is an integer of 15 to 1013, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:174, and where b is	
	greater than or equal to a + 14.	
827565	Preferably excluded from the present invention are	
l	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1683 of SEQ ID	
l .	NO:175, b is an integer of 15 to 1697, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:175, and where b is	
22222	greater than or equal to a + 14.	
827893	Preferably excluded from the present invention are	·
1	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1395 of SEQ ID	
	NO:176, b is an integer of 15 to 1409, where both a	
İ	and b correspond to the positions of nucleotide	į
	residues shown in SEQ ID NO:176, and where b is	
	greater than or equal to a + 14.	
828072	Preferably excluded from the present invention are	R20502, R45322, R45322, H29062,
	one or more polynucleotides comprising a nucleotide	H29165, N36388, N39601, AA043930,
	sequence described by the general formula of a-b,	AA044003, AA115568, AA115087,
	where a is any integer between 1 to 1489 of SEQ ID	AA232982, AA234020, AA251431,
1	NO:177, b is an integer of 15 to 1503, where both a	AA251432, AA459761, AA768137,
j	and b correspond to the positions of nucleotide	AA830696, AA918618, AA977409
]	residues shown in SEQ ID NO:177, and where b is	
020200	greater than or equal to a + 14.	77.000
828228	Preferably excluded from the present invention are	[776992, T83862, R37649, R68086,
	one or more polynucleotides comprising a nucleotide	R68125, H05325, H05379, H11520,
	sequence described by the general formula of a-b,	H60866, N27826, N59149, N71661,
	where a is any integer between 1 to 1364 of SEQ ID	AA004459, AA004512, AA026983,
	NO:178, b is an integer of 15 to 1378, where both a	AA031653, AA045803, AA045870,
	and b correspond to the positions of nucleotide	AA127220, AA126199, AA129772,
	residues shown in SEQ ID NO:178, and where b is	AA133788, AA131742, AA166788,
	greater than or equal to a + 14.	AA216416, AA229513, AA469120,
		AA469189, AA503687, AA516488,
		AA522741, AA542827, AA614664,
		AA847108, AA876618, AA886579,
		AA887825, AA888263, AA888262,
		AA934459, N31217, D79619, N55800,
020241	Professional design of the second sec	AA026982, AA031743
828241	Preferably excluded from the present invention are	R09047, H71262, N28995, W07805,
	one or more polynucleotides comprising a nucleotide	W89157, AA007537, AA203119
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2237 of SEQ ID	
	NO:179, b is an integer of 15 to 2251, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:179, and where b is greater than or equal to a + 14.	
	greater than or equal to a + 14.	L

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828287	Preferably excluded from the present invention are	R00158, R34699, R34806, R55812.
l	one or more polynucleotides comprising a nucleotide	R55897, H02931, H04234, H38596,
}	sequence described by the general formula of a-b.	H38841, H38877, R84345, R84762,
	where a is any integer between 1 to 986 of SEQ ID	R85507, H51401, N22910, N31298,
	NO:180, b is an integer of 15 to 1000, where both a	N36027, N64463, N70710, N80820,
]	and b correspond to the positions of nucleotide	N94519, N99846, W15234, W15579,
	residues shown in SEQ ID NO:180, and where b is	W15620, W23968, W24669, W30920,
l	greater than or equal to a + 14.	W31655, W37399, W37400, W39182,
		W45512, W44342, W45653, W44569,
1		W44608, W47630, W47631, W52183,
		W52421, W57603, W58189, W58466,
		W60614, W73715, W78044, W90451,
Ī		W90258, W92042, W91902,
		AA012954, AA013060, AA013459,
		AA013460, AA018132, AA018050,
		AA021226, AA021359, AA021556,
İ		AA021640, AA033802, AA040580,
	<u>†</u> .	AA040552, AA047883, AA054092,
	•	AA055181, AA055893, AA082252,
		AA082502, AA099128, AA099165,
		AA100988, AA131285, AA136296,
		AA136178, AA151469, AA151470,
]	·	AA156144, AA158033, AA158325,
		AA164422, AA164402, AA167105,
		AA182609, AA182541, AA187289, AA187406, AA523678, AA582094,
		AA570257, AA573999, AA574305,
		AA579097, AA661683, AA662869,
		AA664665, AA736798, AA770689,
		AA865267, AA902336, AA923648,
		AA933570, AA939196, AA988468,
		A1000226, A1089764, D79059, N84733,
		W73650, N86290, N88454, C04677,
		C06015, AA033803, R29541,
		AA089664, AA089996, C17096,
	, , , , , , , , , , , , , , , , , , ,	C17255, C19033, AA093458
828364	Preferably excluded from the present invention are	R55711, R55921, R68105, R68149,
		R72479, R72941, N70480, W72759
	sequence described by the general formula of a-b,	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
	where a is any integer between 1 to 1415 of SEQ ID	
	NO:181, b is an integer of 15 to 1429, where both a	•
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:181, and where b is	
	greater than or equal to a + 14.	
828371		T62048, T62112, T91683, T92364,
	one or more polynucleotides comprising a nucleotide	T92416, T93284, N49690, N49793,
	sequence described by the general formula of a-b,	N64329, N80813, W15549, W15404,
	where a is any integer between 1 to 2711 of SEQ ID	W31643, W53039, W92220, W92342,
	NO:182, b is an integer of 15 to 2725, where both a	AA055521, AA055520, AA149883,
	and b correspond to the positions of nucleotide	AA150063, AA148836, AA150436
	residues shown in SEQ ID NO:182, and where b is	·
	greater than or equal to a + 14.	
828403		AA485171, AA515218, AA603721,
	one or more polynucleotides comprising a nucleotide	AA612760, AA838541, AA970526,
	sequence described by the general formula of a-b,	C18512
	where a is any integer between 1 to 1737 of SEQ ID	
	NO:183, b is an integer of 15 to 1751, where both a	

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	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:183, and where b is	
	greater than or equal to a + 14.	
828501	Preferably excluded from the present invention are	H19145, N75547, AA044653,
	one or more polynucleotides comprising a nucleotide	AA128979, AA159576, AA423963,
ļ.	sequence described by the general formula of a-b,	AA523306, H62675, H97872,
ľ	where a is any integer between 1 to 2186 of SEQ ID	AA610503, AA010941, AA011327,
	NO:184. b is an integer of 15 to 2200, where both a	AA043344
[and b correspond to the positions of nucleotide	· ·
i	residues shown in SEQ ID NO:184, and where b is	
	greater than or equal to a + 14.	
828520	Preferably excluded from the present invention are	H70392, N30525, N30537, AA010769,
	one or more polynucleotides comprising a nucleotide	AA463668. AA927343, AA091744
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1973 of SEQ ID	
	NO:185, b is an integer of 15 to 1987, where both a	·
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:185, and where b is	
	greater than or equal to a + 14.	
828527	Preferably excluded from the present invention are	T39306, T40514, R08857, R08964,
	one or more polynucleotides comprising a nucleotide	R00734, R00735, R13824, R20172,
	sequence described by the general formula of a-b,	R37684, R44959, R44959, H05503,
	where a is any integer between 1 to 1723 of SEQ ID	H17017, H17018, H54295, H54372,
	NO:186, b is an integer of 15 to 1737, where both a	H54503, H67654, H67974, H87993,
	and b correspond to the positions of nucleotide	N33311, N37017, N44843, N55182,
	residues shown in SEQ ID NO:186, and where b is	N75469, N75534, N77241, N93004,
	greater than or equal to a + 14.	W05278, W05327, W45465, W88760,
		W88865, AA010623, AA010624,
		AA234956, AA235130, AA424457,
		AA282705, AA283023, AA283109,
	·	AA481529, AA481595, AA490727,
		AA491218, AA554176, AA614573,
		AA665370, AA687964, AA736921,
		AA765107, AA767430, AA809487,
		AA865595, N88052
828538	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
-	where a is any integer between 1 to 1118 of SEQ ID	
	NO:187, b is an integer of 15 to 1132, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:187, and where b is	
000541	greater than or equal to a + 14.	
828541	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1253 of SEQ ID	
	NO:188, b is an integer of 15 to 1267, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:188, and where b is	
2007/2	greater than or equal to a + 14.	
828549	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3773 of SEQ ID	
	NO:189, b is an integer of 15 to 3787, where both a	
	and b correspond to the positions of nucleotide	<u></u>

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	residues shown in SEQ ID NO:189, and where b is	
	greater than or equal to a + 14.	
828562	Preferably excluded from the present invention are	1
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 540 of SEQ ID	
	NO:190, b is an integer of 15 to 554, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:190, and where b is	
	greater than or equal to a + 14.	
828576	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 860 of SEQ ID	
	NO:191, b is an integer of 15 to 874, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:191, and where b is	ı
	greater than or equal to a + 14.	
828602	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2089 of SEQ ID	
	NO:192. b is an integer of 15 to 2103, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:192, and where b is	
	greater than or equal to a + 14.	
328628	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1303 of SEQ ID	
	NO:193, b is an integer of 15 to 1317, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:193, and where b is	
	greater than or equal to a + 14.	
328667	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1238 of SEQ ID	
	NO:194, b is an integer of 15 to 1252, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:194, and where b is	1
	greater than or equal to a + 14.	
28684	Preferably excluded from the present invention are	D11676 D12204 NG0621 NIZ1675
20004	one or more polynucleotides comprising a nucleotide	R11676, R12284, N68621, N71575,
	sequence described by the general formula of a-b,	N99448, W02008, W58632, W74361,
		W76341, W78934, W85701,
	where a is any integer between 1 to 1674 of SEQ ID	AA070898, AA070787, AA102636,
	NO:195, b is an integer of 15 to 1688, where both a	AA102661, AA102678, AA190864,
	and b correspond to the positions of nucleotide	AA190957, AA197279, AA251577,
	residues shown in SEQ ID NO:195, and where b is	AA464994, AA421724, AA470741,
	greater than or equal to a + 14.	AA505341, AA506137, AA583780,
		AA579967, AA714136, AA743352,
		AA747903, AA814422, AA826755,
		AA836633, AA837944, AA936844,
		AI004160, C00265. AA641021
28727	Preferably excluded from the present invention are	R35925, R35954, R49443, R49468,
	one or more polynucleotides comprising a nucleotide	R49443, R49468, N74960, AA083678,
	sequence described by the general formula of a-b,	AA086366, AA100585, AA111863,

	where a is any integer between 1 to 742 of SEQ ID	AA156573, AA159175. AA192611,
	NO:196. b is an integer of 15 to 756, where both a	AA195925. AA195976. AA418567,
	and b correspond to the positions of nucleotide	AA418582
	residues shown in SEQ ID NO:196, and where b is	
	greater than or equal to a + 14.	
828734	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1457 of SEQ ID	
:	NO:197. b is an integer of 15 to 1471, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:197, and where b is	ļ
	greater than or equal to a + 14.	1
828750	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 678 of SEQ ID	
	NO:198, b is an integer of 15 to 692, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:198, and where b is	1
	greater than or equal to $a + 14$.	1
828842	Preferably excluded from the present invention are	R31695, R31737, R86919, R86763.
	one or more polynucleotides comprising a nucleotide	H66952, N30849, N41376, N95538,
	sequence described by the general formula of a-b,	W03782, W24227, N90171, AA020001,
	where a is any integer between 1 to 1559 of SEQ ID	AA046039, AA046149, AA099753,
	NO:199, b is an integer of 15 to 1573, where both a	AA489705, AA552582, AA580818,
	and b correspond to the positions of nucleotide	AA584291, AA730113, AA910268
	residues shown in SEQ ID NO:199, and where b is	1 1304271, 7171730113, 7171710200
	greater than or equal to a + 14.	
828843	Preferably excluded from the present invention are	T57326, T57387, T94838, T94837,
020043	one or more polynucleotides comprising a nucleotide	T94879, T94925, T74456, R11995,
	sequence described by the general formula of a-b,	R15234, R19543, R21728, R36670,
	where a is any integer between 1 to 2728 of SEQ ID	R39752, R39834, R40808, R40808,
	NO:200, b is an integer of 15 to 2742, where both a	R43895, R70936, R70988, R74057,
	and b correspond to the positions of nucleotide	R74152, R79967, R80062, H02983,
	residues shown in SEQ ID NO:200, and where b is	· ·
	greater than or equal to a + 14.	H04277, H08966, H09537, H25298,
	greater than or equal to a + 14.	H25343, H25449, H25495, H29439,
		H29438, H29887, H29987, R86318, H65676, H87966, H88350, H97859,
		N20316, N26629, N27590, N39724,
		N52972, W39188, W45099, W45149, N90248, AA004834, AA033776,
		AA039900, AA039901, AA041524,
	1	AA044928, AA082729, AA085742,
		AA112974, AA128343, AA133157,
		AA171997, AA418609, AA418664,
		AA421626, AA430065, AA230107,
		AA230108, AA513630, AA521134,
		AA622056, AA635868, AA639882,
		AA714929, AA715480, AA715556,
		AA729814, AA731061, AA811597,
		AA830222, AA873240, AA886078,
		AA886270, AA907208, AA932201.
		14 4 07774477 4 4 4 0 0 0 0 0 0 0 0 0 0 0
		AA977447, AA989000, D81476,
		N56281, C21262, AA089709
828851	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	

		
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1403 of SEQ ID	
	NO:201, b is an integer of 15 to 1417, where both a	·
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:201, and where b is	
	greater than or equal to a + 14.	
828856	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	<u>'</u>
ţ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1498 of SEQ ID	<u>]</u>
	NO:202, b is an integer of 15 to 1512, where both a	
	and b correspond to the positions of nucleotide	1
ı	residues shown in SEQ ID NO:202, and where b is	ì
1	greater than or equal to a + 14.	
828862	Preferably excluded from the present invention are	AA021223
	one or more polynucleotides comprising a nucleotide	11021223
1	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 405 of SEQ ID	
	NO:203. b is an integer of 15 to 419, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:203, and where b is	
	greater than or equal to a + 14.	
828870	Preferably excluded from the present invention are	
020070	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	f
	where a is any integer between 1 to 2819 of SEQ ID	
	NO:204, b is an integer of 15 to 2833, where both a	
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:204, and where b is	
000000	greater than or equal to a + 14.	
828873	Preferably excluded from the present invention are	i
ļ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 5816 of SEQ ID	
1	NO:205, b is an integer of 15 to 5830, where both a	Į.
	and b correspond to the positions of nucleotide	·
[.	residues shown in SEQ ID NO:205, and where b is	
	greater than or equal to a + 14.	<u> </u>
828892	Preferably excluded from the present invention are	R54649, W46198
	one or more polynucleotides comprising a nucleotide	· ·
ļ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 741 of SEQ ID	
	NO:206, b is an integer of 15 to 755, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:206, and where b is	
	greater than or equal to a + 14.	1
828893	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1982 of SEQ ID	
	NO:207, b is an integer of 15 to 1996, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:207, and where b is	
	greater than or equal to a + 14.	
828807		
828897	Preferably excluded from the present invention are	·
	one or more polynucleotides comprising a nucleotide	
<u> </u>	sequence described by the general formula of a-b,	<u> </u>

	where a is any integer between 1 to 1654 of SEQ 1D	1
	NO:208, b is an integer of 15 to 1668, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:208, and where b is	
	greater than or equal to a + 14.	
828910	Preferably excluded from the present invention are	T91595, T65436, T65518, T70584,
	one or more polynucleotides comprising a nucleotide	T70847, T75377, R09159, R09261,
	sequence described by the general formula of a-b,	R09950, T96365, T96446, R12590,
	where a is any integer between 1 to 2236 of SEQ ID	R13068, R18120, R21193, R22430,
	NO:209, b is an integer of 15 to 2250, where both a	R22480, R22810, R25025, R26742,
	and b correspond to the positions of nucleotide	R26976, R32026, R32079, R33017,
	residues shown in SEQ ID NO:209, and where b is	R33904, R36588, R39200, R40499,
	greater than or equal to a + 14.	R45972, R40499, R45972, R56330,
		R64494, R65591, R67446, R70974,
	1	R74477, R74579, R77932, R78301,
		R78497, R78547, R80142, R80143,
	•	H00643, H00729, H03024, H04306,
		H06614, H07124, H09643, H09677,
		H28706, H28835, H42802, H47310,
	•	R92010, H65658, H65657, H67068,
	1	H68151, H71685, H72248, H72786,
		H72785, H73342, H75583, H75514,
		H77433, H98557, N20087, N22979,
		N23822, N28617, N29593, N32509,
		N33262, N40705, N42724, N44752,
		N45195, N57760, N58105, N59101,
		N59726, N64423, N66868, N71993,
		N73995, N99375, W01801, W02025,
		W19280, W19667, W19930, W25451,
		W25645, W31475, W31938, W32153,
		W32005, W37711, W37710, W46758,
		W46905, W49818, W56089, W57771,
	'	W57844, W61375, W61376, W60415,
		W60416, W61142, W61190, W67942,
		W67941, W74649, W84332, W84393,
		W86146, W94323, AA016041,
		AA015933, AA022593, AA022594,
		AA030003, AA043309, AA069392,
		AA069393, AA069775, AA069812,
		AA102392, AA112674, AA112673,
		AA135337, AA135336, AA143448,
		AA152405, AA152459, AA149804,
		AA149829, AA149849, AA149856,
		AA156559, AA157731, AA159045,
		AA160734, AA173662, AA173661,
		AA235812, AA242974, AA243081,
		AA242998, AA252146, AA460003,
		AA460542, AA428205, AA429142,
		AA285041, AA283758, AA283993,
		AA480305, AA506566, AA524852,
		AA631324, AA575859, AA658502,
		AA766717, AA808234, AA837876,
		AA866075, AA877425, AA879058,
		AA886608, AA902179, AA904000,
		AA928667, AA937136, AA962263,
		AA995987, A1024986, W25995,
		W26229, W27231, W26246, W28106,

		W28807. W48809, C01974. AA640952, C14885. C15137
828927	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 824 of SEQ ID NO:210, b is an integer of 15 to 838, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:210, and where b is greater than or equal to a + 14.	
828932	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1199 of SEQ ID NO:211, b is an integer of 15 to 1213, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:211, and where b is greater than or equal to a + 14.	T50679, T51209, T78077, R42605, R48768, R42605, R91277, H61157, W38635, W44738, W46899, W80700, AA017684, AA017707, AA018069, AA019662, AA040254, AA053989, AA054041, AA070137, AA070138, AA074661, AA086354, AA158859, AA223111, AA224210, AA224315, AA232155, AA471047, AA588037, AA720832, AA872503
828933	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 955 of SEQ ID NO:212, b is an integer of 15 to 969, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:212, and where b is greater than or equal to a + 14.	
828941	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide scquence described by the general formula of a-b, where a is any integer between I to 1680 of SEQ ID NO:213, b is an integer of 15 to 1694, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:213, and where b is greater than or equal to a + 14.	
828957	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1196 of SEQ ID NO:214, b is an integer of 15 to 1210, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:214, and where b is greater than or equal to a + 14.	R09987, R16645, R16734, R81727, H58067, H58066, H59815, H59816, H64860, H65458, N70923, W81647, W81187, AA052891, AA053046, AA251319, AA251723, AA262259, AA262870, AA463359, AA463865, AA417918, AA418169, AA480203, AA521273, AA836429, AA858135, AA888105, AA917914, AA937591, AA947712, AA961752, AA973797, A1085881
828963	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1762 of SEQ ID NO:215, b is an integer of 15 to 1776, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:215, and where b is greater than or equal to a + 14.	·
828964	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	

		· · · · · · · · · · · · · · · · · · ·
1	sequence described by the general formula of a-b,	
İ	where a is any integer between 1 to 1404 of SEQ ID	
	NO:216, b is an integer of 15 to 1418, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:216, and where b is	
	greater than or equal to a + 14.	
828966	Preferably excluded from the present invention are	T57322, T57383, R07432, R07433,
	one or more polynucleotides comprising a nucleotide	R24183, R37889, R64196, R64212,
	sequence described by the general formula of a-b,	H10798, H16281, H96182, N24864,
Į.	where a is any integer between 1 to 2186 of SEQ ID	N31801, N31897, N51466, N53607,
	NO:217, b is an integer of 15 to 2200, where both a	N71323, N71374, N71696, N78973,
	and b correspond to the positions of nucleotide	N91801, N99595, N99806, W17338,
	residues shown in SEQ ID NO:217, and where b is	W38617, W44695, W52815, W93325,
	greater than or equal to a + 14.	W95029, AA027074, AA031625,
		AA031706, AA034522, AA101476,
}		AA101477, AA156927, AA157179,
		AA173234, AA196758, AA506558,
İ		AA541561, AA552220, AA573198,
		AA687807, AA732065, AA769029,
1	· · · · · · · · · · · · · · · · · · ·	AA804914, AA858375, AA931935,
	1	AA995830, AI075078, AI075079,
!		AA641307
828967	Preferably excluded from the present invention are	T86194, T99270, R00981, R21065,
	one or more polynucleotides comprising a nucleotide	R28076, R28291, R46245, R46245,
	sequence described by the general formula of a-b,	R61751, R61752, H20415, H41325,
·	where a is any integer between 1 to 1839 of SEQ ID	H46347, H46354, W01107, W96450,
	NO:218, b is an integer of 15 to 1853, where both a	W96548, AA082920, AA192528,
	and b correspond to the positions of nucleotide	AA494252, AA507548, AA604189,
	residues shown in SEQ ID NO:218, and where b is	AA604361, AA614008, AA622126,
	greater than or equal to a + 14.	AA573865, AA578191, AA568157,
	Situation than or equal to a 1 14.	AA780392, AA812241, AA830010,
		AA836096, AA876742, C21216
828977	Preferably excluded from the present invention are	T54853, T55018, T61617, T61701,
	one or more polynucleotides comprising a nucleotide	[771718, T71787, R43855, R43855,
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1079 of SEQ ID	H79047, W23509, W78022, AA028959,
		AA028960, AA035641, AA035749,
		AA040562, AA042827, AA044641,
		AA150059, AA459301, AA459532,
		AA419054, AA532924, AA603462,
	greater than or equal to a + 14.	AA573839, AA863332, AA877269,
828978	D-C	A1016670, A1083871, A1085531
0407/8	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2141 of SEQ ID	
	NO:220, b is an integer of 15 to 2155, where both a	
	and b correspond to the positions of nucleotide	,
	residues shown in SEQ ID NO:220, and where b is	:
220020	greater than or equal to a + 14.	
828979	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1250 of SEQ ID	
	NO:221, b is an integer of 15 to 1264, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:221, and where b is	` <u>.</u>
	greater than or equal to a + 14.	

829001	Preferably excluded from the present invention are	1
027001		
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b.	
		· ·
	where a is any integer between 1 to 2071 of SEQ ID	
	NO:222, b is an integer of 15 to 2085, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:222, and where b is	<u> </u>
	greater than or equal to a + 14.	
829003	Preferably excluded from the present invention are	T56900, T56901, T57894, T57976,
	one or more polynucleotides comprising a nucleotide	T58709, T83854, T83994, T83995,
	sequence described by the general formula of a-b,	T85283, T85493, T85938, T98545.
	where a is any integer between 1 to 2907 of SEQ ID	T98546, R23866, R51491, R51492,
	NO:223, b is an integer of 15 to 2921, where both a	R70815, H06524, H06579, H21400,
	and b correspond to the positions of nucleotide	H22212, H26306, H26465, H40800,
	residues shown in SEQ ID NO:223, and where b is	H42803, H44004, H45104, H45577,
	greater than or equal to a + 14.	R84544. R85933, R95902, R98186,
		R98187, R99129, H51499, H62734,
		H62818, H67266, H67280, H67971,
		H72027, H72028, H86532, H86617,
		H97834, N22060, N22322, N22927,
	1	N23444, N23843, N27358, N27627,
		N31797, N53099, N55505, N55527,
		N62760, N76278, N76994, N81072,
		N99969, W07363, W15385, W30908,
		W32209, W32266, W37612, W39341,
		W45721, W44369, W60688, W60728,
		W74331, W79764, W79508,
		AA010902, AA011007, AA013382,
		AA013383, AA017180, AA018376,
		AA021435, AA128552, AA128295,
		AA161229, AA160487, AA236095,
		AA259037, AA458538, AA428449,
	·	AA491943, AA492101, AA501898,
		AA505736, AA551906, AA552335,
		AA554636, AA564579, AA588897,
		AA593936, AA595710, AA610733,
		AA612690, AA569349, AA570259,
		AA570263, AA573856, AA579746,
		AA658849, AA721609, AA743280,
		AA743326, AA808972, AA831035,
		AA836900, AA887420, AA887859,
		AA970292, AA994943, AA994947,
		AI014465, F19724, N36447, D78889,
		N75198, W37467, W79607, C03008,
		C04753
829016	Preferably excluded from the present invention are	
- •	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 4381 of SEQ ID	
	NO:224, b is an integer of 15 to 4395, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:224, and where b is	
	greater than or equal to a + 14.	,
829027	Preferably excluded from the present invention are	
067061	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3021 of SEQ ID	
	penere a is any integer between 1 to 3021 of 3EQ ID	L

	·	
	NO:225, b is an integer of 15 to 3035, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:225, and where b is greater than or equal to a + 14.	
829028	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1497 of SEQ ID NO:226, b is an integer of 15 to 1511, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:226, and where b is greater than or equal to a + 14.	
829031	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2225 of SEQ ID NO:227, b is an integer of 15 to 2239, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:227, and where b is greater than or equal to a + 14.	T52373, T52446, T65540, T91789, R10959, T84998, R06717, R28502, R48288, R48390, R48442, R54616, R54879, R55311, R55316, R55413, R55418, R72602, R72669, R72946, H15595, H27333, H41543, H37781, R84976, R85050, R88513, R88514, H49052, H49116, H96219, H96754, H97979, N23664, N25056, N26150, N32997, N51857, N54122, W65281, W65277, W72409, W76488, W92510, N91031, AA045475, AA056943, AA057662, AA057806, AA126670, AA127032, AA136891, AA137001, AA158595, AA158989, AA279342, AA604130, AA604929, AA631863, C01812
829034	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2332 of SEQ ID NO:228, b is an integer of 15 to 2346, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:228, and where b is greater than or equal to a + 14.	·
829036	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	W19899, W56172, N91246, AA053015, AA258943, AA508101, AA557537, AA744258, C06034, AA053503
829049	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1988 of SEQ ID NO:230, b is an integer of 15 to 2002, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:230, and where b is greater than or equal to a + 14.	
329073	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	N71827, W07562, W79070, W94296, AA026190, AA215725, AA279902, AA832099

	NO:231, b is an integer of 15 to 994, where both a	
1	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:231, and where b is	
	greater than or equal to a + 14.	
829075	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
ļ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 472 of SEQ ID	
	NO:232, b is an integer of 15 to 486, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:232, and where b is	
	greater than or equal to a + 14.	
829076	Preferably excluded from the present invention are	
]	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 2067 of SEQ ID	
	NO:233, b is an integer of 15 to 2081, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:233, and where b is	
	greater than or equal to a + 14.	
829080	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	,
	where a is any integer between 1 to 502 of SEQ ID	
1	NO:234, b is an integer of 15 to 516, where both a	j
	and b correspond to the positions of nucleotide	1
]	residues shown in SEQ ID NO:234, and where b is	
]	greater than or equal to a + 14.	
829087	Preferably excluded from the present invention are	
029007		<u>.</u>
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	i
	where a is any integer between 1 to 1115 of SEQ ID	
	NO:235, b is an integer of 15 to 1129, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:235, and where b is	<u> </u>
	greater than or equal to a + 14.	
829092	Preferably excluded from the present invention are	
-	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1031 of SEQ ID	
	NO:236, b is an integer of 15 to 1045, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:236, and where b is	
	greater than or equal to a + 14.	
829095	Preferably excluded from the present invention are	T98739, T98740, R53404, R72484,
	one or more polynucleotides comprising a nucleotide	H09731, H16600, H21795, H25680,
	sequence described by the general formula of a-b,	N79773, N93472, AA812105,
	where a is any integer between 1 to 676 of SEQ ID	AA826523, AA954170, AI084914
	NO:237, b is an integer of 15 to 690, where both a	1 10000
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:237, and where b is	
	greater than or equal to a + 14.	
		T40001 T40020 P52055 P55000
92000	back-and to an about a fear with the second in the second in	
829096	Preferably excluded from the present invention are	T40001, T40939, R53257, R62981,
829096	one or more polynucleotides comprising a nucleotide	R62980, R63036, H15127, H15187,
829096	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	R62980, R63036, H15127, H15187, H24078, H24188, H81472, H88927,
829096	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	R62980, R63036, H15127, H15187,

		II . aaaaaa aaa aa aa aa aa aa aa
	and b correspond to the positions of nucleotide	AA022965. AA024917, AA024918.
ŀ	residues shown in SEQ ID NO:238, and where b is	AA035721. AA062907. AA102646,
	greater than or equal to a + 14.	AA101299. AA223395, AA419511.
	ſ	AA421963, AA421964, AA524699,
	·	AA532380, AA614315, AA570194,
		AA742712, AA865440, AA887301,
020110	D C 11 111C 11	AA987486, AA988144, AA091175
829118	Preferably excluded from the present invention are	·
ĺ	one or more polynucleotides comprising a nucleotide	
•	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 891 of SEQ ID	
	NO:239, b is an integer of 15 to 905, where both a	
]	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:239, and where b is	
ł	greater than or equal to a + 14.	
829152	Preferably excluded from the present invention are	T72498, T73568, T74363, T86984,
	one or more polynucleotides comprising a nucleotide	R10378, R10477, T85969, R05924,
ĺ	sequence described by the general formula of a-b,	R06022, H58205, H65999, H66000,
1		1
	where a is any integer between 1 to 1470 of SEQ ID	N68870, N92084, N92944, AA188651,
1	NO:240, b is an integer of 15 to 1484, where both a	AA188754, N72345
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:240, and where b is	
	greater than or equal to a + 14.	
829160	Preferably excluded from the present invention are	R19077, R24890, R70937, R70989,
,	one or more polynucleotides comprising a nucleotide	R75822, R75823, H13581, R88030,
1	sequence described by the general formula of a-b,	H97197, H97205, H97610, H97622,
ŀ	where a is any integer between 1 to 1507 of SEQ ID	H97640, H99011, N22163, N22211,
ļ	NO:241, b is an integer of 15 to 1521, where both a	N25706, N31618, N31627, N34096,
ļ	and b correspond to the positions of nucleotide	N35586, N57066, N57078, N57083,
	residues shown in SEQ ID NO:241, and where b is	N63961, N71248, N71530, N79638,
	greater than or equal to a + 14.	W23686, W25345, W80523, W80524,
	1	AA027117, AA044025, AA044347,
1		
	1.	AA056543, AA056646, AA082122,
		AA120870, AA120871, AA129173,
,		
,		AA120870, AA120871, AA129173, AA129197, AA173547, AA173713,
		AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865,
		AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606,
829163	Preferably excluded from the present invention are	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224
829163	Preferably excluded from the present invention are	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848,
829163	one or more polynucleotides comprising a nucleotide	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224
829163	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848,
829163	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848,
829163	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848,
829163	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848,
829163	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14.	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877
829163 829176	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID NO:243, b is an integer of 15 to 934, where both a	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713, N68598, N71315, N71366, N99798,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID NO:243, b is an integer of 15 to 934, where both a and b correspond to the positions of nucleotide	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID NO:243, b is an integer of 15 to 934, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:243, and where b is	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713, N68598, N71315, N71366, N99798,
829176	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID NO:243, b is an integer of 15 to 934, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:243, and where b is greater than or equal to a + 14.	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713, N68598, N71315, N71366, N99798, W01984
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID NO:243, b is an integer of 15 to 934, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:243, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713, N68598, N71315, N71366, N99798, W01984 R50489, R50573, R74498, R74499,
829176	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1130 of SEQ ID NO:242, b is an integer of 15 to 1144, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 920 of SEQ ID NO:243, b is an integer of 15 to 934, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:243, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	AA120870, AA120871, AA129173, AA129197, AA173547, AA173713, AA190689, AA252595, AA258865, AA259007, AA576323, AA768606, N55993, N84224 R27150, H50951, N39917, N41848, N41877 T46875, T53785, T62036, T73807, R11065, R11122, T84299, T85183, R01714, R02656, R02737, R02738, H41134, H64904, H79712, H79713, N68598, N71315, N71366, N99798, W01984

	where a is any integer between 1 to 901 of SEQ ID	
	NO:244, b is an integer of 15 to 915, where both a	
ļ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:244, and where b is	·
2222	greater than or equal to a + 14.	
829207	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
i	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1262 of SEQ ID	į
	NO:245, b is an integer of 15 to 1276, where both a	
١	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:245, and where b is	
	greater than or equal to a + 14.	
829228	Preferably excluded from the present invention are	T40764, T49773, T49774, H05098,
	one or more polynucleotides comprising a nucleotide	H49148, H51985, H52105, N36154,
l	sequence described by the general formula of a-b,	N51490, N52526, N53635, AA054314,
	where a is any integer between 1 to 3352 of SEQ ID	AA074167, AA152473, AA152472,
	NO:246, b is an integer of 15 to 3366, where both a	AA188950, AA278366, AA281330,
l	and b correspond to the positions of nucleotide	AA468930, AA469004, AA482010,
	residues shown in SEQ ID NO:246, and where b is	AA542938, AA554491, AA565215,
	greater than or equal to a + 14.	AA579406, AA741363, AA807139,
		AA832066, AA836995, AA876036,
		AA995854
829252	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2134 of SEQ ID	
	NO:247, b is an integer of 15 to 2148, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:247, and where b is	
	greater than or equal to a + 14.	
829254	Preferably excluded from the present invention are	
027234	one or more polynucleotides comprising a nucleotide	•
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2211 of SEQ ID	
	NO:248, b is an integer of 15 to 2225, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:248, and where b is	
	greater than or equal to a + 14.	
829269		
047409	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	•
	where a is any integer between 1 to 1190 of SEQ ID	
	NO:249, b is an integer of 15 to 1204, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:249, and where b is	
2222	greater than or equal to a + 14.	
829277	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1300 of SEQ ID	
	NO:250, b is an integer of 15 to 1314, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:250, and where b is	
	greater than or equal to a + 14.	<u> </u>
329290	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	

	bogues described by the second for the first	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1145 of SEQ ID	
	NO:251, b is an integer of 15 to 1159, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:251, and where b is	
829294	greater than or equal to a + 14.	
029294	Preferably excluded from the present invention are	·
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2474 of SEQ ID	
	NO:252. b is an integer of 15 to 2488, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:252, and where b is	
020200	greater than or equal to a + 14.	T00004 1705(10 1740006 11170104
829299	Preferably excluded from the present invention are	T82894, H25618, N48726, W52191,
	one or more polynucleotides comprising a nucleotide	AA037331, AA223798, AA224330,
	sequence described by the general formula of a-b.	AA635842, AA748884, AA826495,
	where a is any integer between 1 to 1540 of SEQ ID	AA864458, AA903250, AA908466,
[NO:253. b is an integer of 15 to 1554, where both a	AA931986, D81481, N56293, C02225
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:253, and where b is	
020200	greater than or equal to a + 14.	D13070 D17370 D40000 D4000
829308	Preferably excluded from the present invention are	R13979, R17378, R40039, R42616,
	one or more polynucleotides comprising a nucleotide	R42616, R40039, R56257, R56346,
	sequence described by the general formula of a-b,	H05467, H07018, R86778, H99527,
	where a is any integer between 1 to 1492 of SEQ ID	H99526, H99763, N24571, N25539,
	NO:254, b is an integer of 15 to 1506, where both a	N25635, N28490, N30121, N34013,
	and b correspond to the positions of nucleotide	N34136, N34233, N35730, N49189,
	residues shown in SEQ ID NO:254, and where b is	N50244, N92737, W20356, AA255602,
	greater than or equal to a + 14.	AA262707, AA255576, AA262183,
i		AA279758, AA570002, AA572777,
		AA721016, AA814424, AA864521,
		AA902860, AA948310, AI024777,
000040		A1056401
829349	Preferably excluded from the present invention are	T39288, T47082, T50451, T50586,
	one or more polynucleotides comprising a nucleotide	T59000, T59073, T59535, T59586,
	sequence described by the general formula of a-b,	T63704, T63861, T69920, T69974,
	where a is any integer between 1 to 640 of SEQ ID	T71240, T72474, T72943, T90268,
,	NO:255, b is an integer of 15 to 654, where both a	T90710, T83786, T95048, R31368,
	and b correspond to the positions of nucleotide	R33435, R34369, R34489, R73911,
	residues shown in SEQ ID NO:255, and where b is	R80467, R80667, R94351, R97310,
	greater than or equal to a + 14.	R97345, H57329, H57376, H62783,
		H64845, H65444, H82981, H83214,
		H93955, H93956, N29780, N42940,
		N45379, N57200, N80805, W06876,
	· ·	W15396, W47162, W47283, W52164,
		W52024, W52758, W73045, W73275,
		W73604, W73643, W86783, W87274,
		AA009954, AA010849, AA011288,
		AA022621, AA022757, AA025805,
	•	AA025929, AA025968, AA046835,
		AA054475, AA058513, AA063327,
		AA075215, AA075451, AA088739,
		AA088740, AA099371, AA099457,
		AA112397, AA113053, AA121065,
		AA121066, AA132025, AA132147,
		AA132237, AA132357, AA146935,

		AA147721, AA147756, AA147602,
1		AA148113, AA156063, AA157120,
1		AA157223, AA157610, AA165107,
		AA164710. AA173741, AA173185,
		AA187331, AA187332, AA187293,
ľ		AA187393, AA187741, AA188097.
İ		AA187033, AA188455, AA188457,
1		AA188467, AA216356, AA228668,
1		AA229001, AA228993, AA229108,
		AA397406, AA482922, AA483319,
1		AA483431, AA491567, AA501502,
		AA507889, AA508445, AA513947,
1		AA515053, AA522563, AA523140,
1		AA525478, AA524922, AA526106.
		AA534088, AA535846, AA548219,
1		AA552477, AA555012, AA558315,
		AA564882, AA565458, F16817.
1		F16991, F17527, AA582793,
1		AA587225, AA588487, AA595626,
İ		AA602055, AA602240, AA603392,
		AA631634, AA638971, AA633988,
1		AA640535, AA576051, AA576894.
		AA566049, AA655021, AA659001,
		AA661609, AA662354, AA664631.
İ		AA664721, AA664980, AA665338,
		AA688035, AA714993, AA715012, AA720861, AA730373, AA730633,
1		AA742678, AA742934, AA746812,
1	•	
		AA747153, AA747192, AA747959,
1		AA808437, AA836880, AA837645,
Ì		AA838637, AA872341, AA876822,
İ		AA922665, AA961515, AA968734,
}	•	AA970649, AA978219, AA988051,
		AA988404, AA991418, AA994111,
1		A1002489, A1053409, A1053609,
		A1053760, A1082351, A1083631,
		N83854, N83948, N85971, N86260,
1	· ·	N86628, N87758, AA641679,
1		AA642097, AA642839, C20758,
829354	Professibly evaluded from the account investigation	AA092159, AA092465, AA094493
027334	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b, where a is any integer between 1 to 1978 of SEQ ID	
]		
	NO:256, b is an integer of 15 to 1992, where both a and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:256, and where b is	:
	greater than or equal to a + 14.	
829388	Preferably excluded from the present invention are	
027300	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2259 of SEQ ID	
	NO:257, b is an integer of 15 to 2273, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:257, and where b is	
920640	greater than or equal to a + 14.	N124400 N120020 N120020 N12455
829540	Preferably excluded from the present invention are	N26408, N28830, N28838, N31522,

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1490 of SEQ ID NO:258, b is an integer of 15 to 1504, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:258, and where b is	W15157, W81560, W81561, AA126749, AA126756, AA126772, AA187148
00000	greater than or equal to a + 14.	
829626	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1778 of SEQ ID NO:259, b is an integer of 15 to 1792, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:259, and where b is	·
829730	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2034 of SEQ ID NO:260, b is an integer of 15 to 2048, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:260, and where b is greater than or equal to a + 14.	
829892	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1268 of SEQ ID NO:261, b is an integer of 15 to 1282, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:261, and where b is greater than or equal to a + 14.	R84306, N99830, N90467, AA113938, AA192541, AA243317, L44546, AA713588
829933	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 585 of SEQ ID NO:262, b is an integer of 15 to 599, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:262, and where b is greater than or equal to a + 14.	AA121059, AA429187
829938	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1247 of SEQ ID NO:263, b is an integer of 15 to 1261, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:263, and where b is greater than or equal to a + 14.	AA001837, AA142857, AA235114, AA235222, AA614412, AA687460, AA857702, AA857893, AA962131, AA962521
829969	Preferably excluded from the present invention are	R22931, R23036, H09755, H47088, N38971, N38985, N57545, AA075344, AA075597, AA136299, AA136180, AA279124, AA279243, AA279928, AA279929, AA909786, AI000293, N48117, N48131
829982	Preferably excluded from the present invention are	H40097, N80803, N93871, W07650,
		W15482, W40363, W42635, W45238,

	sequence described by the general formula of a-b, where a is any integer between 1 to 557 of SEQ ID NO:265, b is an integer of 15 to 571, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:265, and where b is greater than or equal to a + 14.	W67482, W67483. W70331. W72456, W73235, W73290. W76515. W78220, AA040927, AA040928. AA074829, AA075095, AA083686. AA166708. AA167049, AA228843. AA468686, AA469044, AA505509. AA548788, AA564157, AA595572. AA622149, AA633298, AA576799. AA746697. AA807946, AA873193, AA903706, AA919114. AA932502, AA938506, AA974058, AA977996, A1000750, N85073. N86741, N87037, N88197, N88746, AA090569
830007	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1336 of SEQ ID NO:266, b is an integer of 15 to 1350, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:266, and where b is greater than or equal to a + 14.	
830019	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1305 of SEQ ID NO:267, b is an integer of 15 to 1319, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:267, and where b is greater than or equal to a + 14.	T61424, T53868, T61391, T63785, R23153, R23154, R23905, R64468, R65575, R69390, R69523, R79153, R79154, H14532, H14533, H47318, H47402, H53647, H61347, H93017, H94242, N29789, N42932, W57927, W58148, W67701, W68160, W74342, W81702, W81703, W94692, W95218, W95440, W95785, AA043712, AA056570, AA114073, AA133633, AA133634, AA151774, AA149729, AA149782, AA149782, AA149782, AA425861, AA425990, AA428095, AA428642, AA494401, AA515475, AA523534, AA548827, AA552032, AA564916, F16977, AA593645, AA613557, AA617694, AA618542, AA576565, AA576574, AA746168, AA766359, AA833956, AA837906, AA857421, AA857877, AA903383, AA903849, AA903888, AA916517, AA922889, AA962544, AA977534, AA974964, AA975402, AA976089, AA983583, AA992448, F18477, C04429, C17306
830073	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3680 of SEQ ID NO:268, b is an integer of 15 to 3694, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:268, and where b is greater than or equal to a + 14.	T93694, T96159, H04182, H04181, H15428, H48586, N74976, W05676, W44928, AA085826, AA085971, AA126446, AA425304, AA425408, AA280817, AA280995, AA287270, AA287417, AA668788, AA836455, AA977754
830130	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1228 of SEQ ID	

	NO:269, b is an integer of 15 to 1242, where both a	
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:269, and where b is	·
	greater than or equal to a + 14.	
830134	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 2043 of SEQ ID	
	NO:270, b is an integer of 15 to 2057, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:270, and where b is	, '
<u></u>	greater than or equal to a + 14.	
830135	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 946 of SEQ ID	;
	NO:271, b is an integer of 15 to 960, where both a	
1	and b correspond to the positions of nucleotide	
į	residues shown in SEQ ID NO:271, and where b is	
<u> </u>	greater than or equal to a + 14.	
830148	Preferably excluded from the present invention are	R15244, R31943, R31992, H06853,
	one or more polynucleotides comprising a nucleotide	H06894, H13355, H30882, R84410,
	sequence described by the general formula of a-b,	R84411, R94120, H53381, H97695,
j	where a is any integer between 1 to 1153 of SEQ ID	H99925, N46996, N69023, N77897,
	NO:272, b is an integer of 15 to 1167, where both a	W00690, W19694, W38937, W74721,
	and b correspond to the positions of nucleotide	W74795, N89822, N89950, AA009490,
l	residues shown in SEQ ID NO:272, and where b is	AA009904, AA031349, AA031350,
ŀ	greater than or equal to a + 14.	AA035629, AA035719, AA046140,
}	· ·	AA062845, AA062905, AA079564,
1		AA079636, AA116062, AA116046,
		AA126968, AA148568, AA159591,
1		AA160429, AA161272, AA161273,
		AA160576, AA179774, AA180491,
		AA179635, AA182631, AA182727,
		AA179634, AA192371, AA192282,
		AA199831, AA251312, AA256883,
		AA255477, AA430121, AA533720,
ļ		AA551694, AA552307, AA552661,
		AA582138, AA586611, AA587906,
		AA594387, AA602977, AA605299,
		AA633388, AA573941, AA574038,
		AA579715, AA687647, AA741352,
		AA838339, AA857603, AA858082,
		AA866081, AA865003, AA875861,
		AA910672, AA927563, AI076918,
		W21962
830149	Preferably excluded from the present invention are	R60249, R60762, R63751, R67526,
[]		H95029, H95095, N59347, N77158,
	sequence described by the general formula of a-b,	W19778, AA047615, AA047555,
	where a is any integer between 1 to 2757 of SEQ ID	AA047687, AA047738, AA056453,
	NO:273, b is an integer of 15 to 2771, where both a	AA070880, AA112293, AA113105,
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:273, and where b is	AA112550, AA112614, AA158015,
		AA158228, AA160995, AA160996,
	greater than or equal to a + 14.	AA190555, AA191131, AA224574,
		AA227422, AA255563, AA255586,
		AA418477, AA424689, AA470392,
	<u></u>	AA515485, AA515507, AA583475,

		AA588210, AA602533, AA573902, AA568354. AA746111, AA766146,
ļ		AA804893. N83302
830154	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1875 of SEQ ID	
	NO:274, b is an integer of 15 to 1889, where both a	
ļ	and b correspond to the positions of nucleotide	
ì	residues shown in SEQ ID NO:274, and where b is	·
222122	greater than or equal to a + 14.	
830183	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 590 of SEQ ID	Ì
	NO:275, b is an integer of 15 to 604, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:275, and where b is	
020104	greater than or equal to a + 14.	
830194	Preferably excluded from the present invention are	T51023, T51115, T52795, T53595,
	one or more polynucleotides comprising a nucleotide	T56300, T56767, T59691, T59827,
	sequence described by the general formula of a-b,	T59904, T63354, T72200, T72269,
	where a is any integer between I to 1367 of SEQ ID	T92900, T92990, R07165, R07217,
	NO:276, b is an integer of 15 to 1381, where both a	R44334, R49609, R44334, R49609,
	and b correspond to the positions of nucleotide	H11106, H20800, H22618, H42472,
	residues shown in SEQ ID NO.276, and where b is	H43453, H50320, H50321, H69947,
	greater than or equal to a + 14.	N20118, N21306, N26128, N63140,
	·	N67225, N67232, W45407, W56419,
		W56420, W72419. W76279, W94626,
		W94710, AA029459, AA029524,
		AA034511, AA035053, AA035563,
		AA039819, AA041465, AA053002,
		AA055974, AA056002, AA070356,
		AA070320, AA074029, AA074039,
		AA074189, AA074336, AA075645,
		AA075646, AA076380, AA084435,
		AA084465, AA084453, AA085290,
		AA086454, AA099172, AA101922,
		AA101959, AA099618, AA102011,
		AA112794, AA126226, AA126304,
		AA128510, AA129955, AA133875, AA128443, AA133328, AA133403,
		AA134003, AA130990, AA131028,
	·	AA132940, AA135158, AA135628,
		AA143273, AA146730, AA151853,
		AA155641, AA155696, AA155726,
		AA157967, AA158903, AA158902,
•		AA158943, AA158944, AA159293,
		AA159526, AA161206, AA160558,
		AA160739, AA160740, AA165357,
		A 167787 A 4160219 A 4160612
		AA167787, AA169218, AA169512,
		AA169691, AA176365, AA179272,
		AA179388, AA180903, AA181001,
		AA181325, AA181508, AA182781,
		AA173899, AA187757, AA188120,
		AA186725, AA187070, AA187152,
		AA190896, AA199819. AA223210,

		AA223254. AA227038, AA232399,
		AA233288. AA243192. AA252285,
		AA492525, AA420611, AA420688,
1		AA492171, AA492254, AA503950,
		AA507398, AA513704, AA513757,
		AA515944, AA525799, AA558212,
	·	AA563863, AA565107, F17110,
		AA582829, AA586678, AA603895,
1		AA604163, AA568617, AA617883,
ŀ		AA622814, AA635987, AA569079,
		AA570078, AA570258, AA570419,
1		AA573205, AA573965, AA574048,
1		AA566065, AA748781, AA834135,
		AA837022, AA838454, AA838636,
ļ		AA838049, AA838058, AA856831,
1		AA909853, AA910298, AA927706,
		AA932101, AA937900, AA953604,
		AA969555, AA973234, AA978074,
		AA985430, AA985432, AA988742,
		AA994207, A1002611, A1014411,
j		N84537, N85082. W22113, W22114,
		W22431, W22639, W23207, W23271,
	·	W29046, N88675, AA640915,
		AA092777
830207	Preferably excluded from the present invention are	R51744, R88177, W05323, AA746479,
	one or more polynucleotides comprising a nucleotide	AA761644, AA826038, W27619,
	sequence described by the general formula of a-b,	AA642452
	where a is any integer between 1 to 1135 of SEQ ID	
	NO:277, b is an integer of 15 to 1149, where both a	
	and b correspond to the positions of nucleotide	
ļ.	residues shown in SEQ ID NO:277, and where b is	·
	greater than or equal to a + 14.	
830242	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 797 of SEQ ID	
	NO:278, b is an integer of 15 to 811, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:278, and where b is	
	greater than or equal to a + 14.	
830328	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1246 of SEQ ID	
l	NO:279, b is an integer of 15 to 1260, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:279, and where b is	
222242	greater than or equal to a + 14.	
830340	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 1654 of SEQ ID	
1	NO:280, b is an integer of 15 to 1668, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:280, and where b is	
93034	greater than or equal to a + 14.	T62005 T62226 T71011 M66677
830341	Preferably excluded from the present invention are	T62985, T63236, T71911, T66677,

	· , ·	
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b. where a is any integer between 1 to 2314 of SEQ ID NO:281. b is an integer of 15 to 2328, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:281, and where b is greater than or equal to a + 14.	T66678, T80777. T81178. R16218, R16219, R67281, H15642. H15643. R96139, R96356. H61487. H61952, H62021. H62022, H62510, H62577. H62887, H63016. H65659, H65660. H72388, H72834, H80906. H97768. N30162, N35776, N52509, N66853, W44421, AA004323, AA004410, AA025214, AA026003, AA0440205. AA040849, AA079158, AA079159. AA137066, AA137080, AA137137.
		AA136971, AA193479, AA532656, AA602312, AA828635, AA872751, AA934418, D80729, C15337
830351	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 942 of SEQ ID NO:282, b is an integer of 15 to 956, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:282, and where b is greater than or equal to a + 14.	
830358	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1388 of SEQ ID NO:283, b is an integer of 15 to 1402, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:283, and where b is greater than or equal to a + 14.	·
830390	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 661 of SEQ ID NO:284, b is an integer of 15 to 675, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:284, and where b is greater than or equal to a + 14.	
830400	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1325 of SEQ ID NO:285, b is an integer of 15 to 1339, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:285, and where b is greater than or equal to a + 14.	T40239, T41103, T60782, T61153, T92326, T95403, R16530, R16587, R46049, R49231, R49231, R46049, H26122, H26387, H67872, H67872, H97917, N23194, N29748, N57652, N64158, N67587, N77509, N80178, W03502, W23838, W57929, W72584, AA011087, AA011088, AA070667, AA074878, AA075068, AA075019, AA076166, AA079857, AA082235, AA099016, AA099093, AA100754, AA113152, AA126886, AA128207, AA126932, AA128546, AA130882, AA136302, AA136408, AA143052, AA143693, AA148079, AA149931, AA151001, AA151091, AA155761, AA157290, AA160781, AA165535, AA173281, AA179903, AA180211, AA181162, AA181673, AA181986.

		AA187551, AA191657, AA192202.
		AA196746, AA196944, AA223166.
		AA224485, AA242866, AA397377,
		AA468734, AA514807, AA523669.
		AA534165, AA534195, AA565551.
·		AA565552, H67199, AA581627.
ł		AA588734, AA588752, AA593857,
1		AA595407. AA595555, AA603965,
i		AA610486, AA614617, AA631563,
1		AA635960, AA636057, AA576256,
1		AA577470, AA580124, AA580480,
		AA714208, AA728790, AA729276.
		AA729361, AA744895, AA745002,
		AA746940, AA746948, AA747346,
1	'	AA804602, AA810873, AA833970,
		AA836938, AA838563, AA858405,
1		AA872330, AA922975, AA946823,
1		AA954185, AA962678, AA978008,
1		AA985504, AA987717, A1004904,
	<u>'</u>	A1017374, A1075264, F19611,
		A1017374, A1073204, F19011, A1089951, N83301, AA082282,
		AA091465, AA093298, AA094459
830437	Preferably excluded from the present invention are	MAU91403, MAU93298, MAU94439
030437	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
<u> </u>	where a is any integer between 1 to 1384 of SEQ ID	
1	NO:286, b is an integer of 15 to 1398, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:286, and where b is	
	greater than or equal to a + 14.	
830458	Preferably excluded from the present invention are	T47583, T47584, T49761, T50148,
050150	one or more polynucleotides comprising a nucleotide	T50203, T47161, R11382, R14878,
]	sequence described by the general formula of a-b,	H18220, H18258, R92715, N78687,
	where a is any integer between 1 to 912 of SEQ ID	W20222, W58210, W58319, W72115,
	NO:287, b is an integer of 15 to 926, where both a	W77801, W79332, W79431, W79487,
	and b correspond to the positions of nucleotide	W79631, W94437, N90582, AA043441,
	residues shown in SEQ ID NO:287, and where b is	AA043442, AA148009, AA147947,
	greater than or equal to a + 14.	AA150837, AA224863, AA225964,
	Broater than or equation 114.	AA226110, AA259194, AA259193,
		AA420769, AA420829, AA470787,
		AA493672, AA501962, AA502082,
		AA506908, AA528607, AA588435,
		AA603500, AA603814, AA627229,
		AA627233, AA627240, AA632058,
		AA632689, AA639239, AA579023,
		AA580698, AA662633, AA661967,
		AA665215, AA729443, AA730546, AA737851, AA745424, AA745526,
		AA747036, AA878568, AA879157,
,		AA886627, AA902180, AA922294,
		AA933050, AA962580, AA977360,
		AA985679, AA996058, AA996145,
	į	A1053546, A1085892, N83274,
	}	
		W15194, N88934, C04128, AA640839,
		AA091328, AA093116, AA094048,
830466	Preferably excluded from the present invention are	, , , , , , , , , , , , , , , , , , , ,

	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
ļ	where a is any integer between 1 to 3080 of SEQ ID	
	NO:288, b is an integer of 15 to 3094, where both a	
1	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:288, and where b is	
Ì	greater than or equal to a + 14.	
830497	Preferably excluded from the present invention are	T47088, T47089, T58430, T58462,
	one or more polynucleotides comprising a nucleotide	R00971, H42144, N77388, W51953,
Į	sequence described by the general formula of a-b,	W52502, AA036671, AA114976,
,	where a is any integer between 1 to 1969 of SEQ ID	AA593693, AA575857, C01052
	NO:289, b is an integer of 15 to 1983, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:289, and where b is	
	greater than or equal to a + 14.	*
830511	Preferably excluded from the present invention are	
030311	one or more polynucleotides comprising a nucleotide	ļ
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1284 of SEQ ID	
	NO:290, b is an integer of 15 to 1298, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:290, and where b is	
020512	greater than or equal to a + 14.	
830512	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2445 of SEQ ID	
	NO:291, b is an integer of 15 to 2459, where both a	.
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:291, and where b is	
	greater than or equal to a + 14.	
830513	Preferably excluded from the present invention are	}
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 556 of SEQ ID	
ł	NO:292, b is an integer of 15 to 570, where both a	
	and b correspond to the positions of nucleotide	
į.	residues shown in SEQ ID NO:292, and where b is	
	greater than or equal to a + 14.	
830540	Preferably excluded from the present invention are	T66458, T98908, R15832, R21916,
	one or more polynucleotides comprising a nucleotide	R22565, H12306, R99043, H57499,
	sequence described by the general formula of a-b,	H82961, AA046203, AA046283,
	where a is any integer between 1 to 2454 of SEQ ID	AA055081, AA055141, AA173411,
	NO:293, b is an integer of 15 to 2468, where both a	AA173467, AA173996, AA176693
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:293, and where b is	
	greater than or equal to a + 14.	
830550	Preferably excluded from the present invention are	R50040, R60172, R71512, H09125,
	one or more polynucleotides comprising a nucleotide	H09475, H21789, R84538, R85928,
	sequence described by the general formula of a-b,	R94762, R96633, R96680, R97580,
	where a is any integer between 1 to 1066 of SEQ ID	H53135, H53241, H82960, H83191,
	NO:294, b is an integer of 15 to 1080, where both a	N68166, N68684, N77903, N80174,
	and b correspond to the positions of nucleotide	N80625, N92442, N93242, N93314,
	residues shown in SEQ ID NO:294, and where b is	N98261, W03498. W05839, W20000,
	greater than or equal to a + 14.	W25100, W31279, W37087, W60751,
		W67554, W67583, W73877, W77814,
		W80412, W95868, W95954, N91343,
		1, 1170000, 1170704, 1171343,

A A026891, A026892, A033347, A034170, A069175, A0884313, AA810170, AA069175, A0884313, AA151307, AA161037, AA251720, AA251726, AA251726, AA251726, AA251726, AA251726, AA251726, AA251726, AA26848, AA429940, AA287366, AA287504, AA470991, AA470994, AA35172, AA46848, AA429940, AA287363, AA569954, AA35172, AA587111, AA602517, AA603483, AA569955, AA732412, AA737913, AA816704, AA838172, AA95896, AA915992, AA948498, AA983538, AA9915992, AA948498, AA983538, AA9915992, AA948498, AA983538, AA9915992, AA948498, AA983538, AA9915992, AA948498, AA983538, AA9915992, AA948498, AA983538, AA9915992, AA948498, AA983538, AA9915992, AA948498, AA983867, AA915995, AA732412, AA737913, AA815731, AA915896, AA915992, AA948498, AA983867, AA91596, AA78184, AA28733, AA857434, AA91586, AA888674, AA91596, AA78184, AA287593, AA291332, AA831433, AA887343, AA8385210, AA834534, AA28366, AA888680, AA818350, AA826203, AA834333, AA887366, AA918645, AA972761, N88184 8300567 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14. 8300586 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 8300587 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 8300588 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830058 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830058 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297			
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A4299940, AA287366, AA287504, AA287504, AA470593, AA716934, AA51493, AA564438, H67293, AA582501, AA583172, AA587111, AA602517, AA603483, AA569955, AA732412, AA737913, AA810504, AA832193, AA857743, AA915872, AA915896, AA915992, AA948498, AA983538, AA991546, AI052409, AI053921, AB587743, AA915872, AA915896, AA915992, AA948498, AA983538, AA991546, AI052409, AI053921, AB587743, AA915872, AA915896, AA915992, AA948498, AA983538, AA991546, AI052409, AI053921, AB587743, AA915872, AA915896, AA915892, AA948498, AA983538, AA991546, AI052409, AI053921, AB5877438, AA083867, AA91580, AB58774, AA9158, AA683867, AA91580, AA918667, AA918746, AA9			
A470593, AA470594, AA514493, AA552301, AA564438, H6793, AA582501, AA583172, AA587111, AA602517, AA603483, AA569955, AA732412, AA737913, AA810504, AA832193, AA837743, AA911872, AA911882, AA91586, AA911992, AA948498, AA933538, AA991546, AI052409, A1053921 830567 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2681 of 5EQ ID NO.295, b is an integer of 15 to 2695, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.295, and where b is greater than or equal to a + 14. 830586 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1380 of SEQ ID NO.296, b is an integer of 15 to 1394, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.296, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO.296, and where b is greater than or equal to a + 14. 830630 Preferably excluded from the present invention are one or more polynucleotides comprising an incleotide residues shown in SEQ ID NO.297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising an incleotide residues shown in SEQ ID NO.297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are not more polynucleotides comprising an incleotide residues shown in SEQ ID NO.297, and where b is greater than or equal to a + 14. 830633 Preferably excluded from the present invention are not more polynucleotides comprising an incleotide residues shown in SEQ ID NO.297, and where b is greater than or equal to a + 14. 830634 Preferably excluded from the present inv	1		
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A7831/7. AA587111. AA602517, AA603483, AA569955, AA732412, AA737913, AA810304, AA832193, AA837743, AA915872, AA915896, AA91592, AA948498, AA935338, AA991546, AI0522409, AI053921 R69708, R75813, R75814, N22294, Where a is any integer between 1 to 2681 of SEQ ID NO:295, b is an integer of 15 to 2695, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14. 830586 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1380 of SEQ ID NO:295, b is an integer of 15 to 1394, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14. 8300586 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 8300632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 8300632 Tarrian or equal to a + 14. 8300632 Tarrian or equal to a + 14. 8300632 Tarrian or equal to a + 14. 8300634 Rosport, AA102188, AA048821, AA99384, AA838521, AA954880, Alo89939 Tarrian or equal to a + 14. 8300637 Tarrian or equal to a + 14. 8300638 Rosport, AA102188, AA048861, AA99173, AA102188, AA048661, AA99384, AA838521, AA9945480, AA99384, AA838521, AA9945480, AA99399 Tarrian or equal to a + 14. Rosport, AA102188, AA164772, AA188544, AA63666, AA311450, AA89984, AA838521, AA9945880, AA99399 Tarrian or equal to a + 14. Rosport, AA102188, AA164772, AA188544, AA63666, AR377, R1682, AA99173, AA102188, AA164772, AA188544, AA63666, AR377, R1682, AA991844, AA838541, AR36874, AA89898, R89938, R893321, R19313, AR36998, R86803, AR39331, R93290, AA962771, AA083844, AA023658, AA029588, AA062771, A			
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Report Rysellade from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2681 of SEQ ID NO:295, b is an integer of 15 to 2695, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14. Report Rysellade from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1380 of SEQ ID NO:296, b is an integer of 15 to 1394, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. Report Rysellade from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. Report Rysellade from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. Report Rysellade Rysellade from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Report Rysellade Rysella			
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 268 of SEQ ID NO:295, b is an integer of 15 to 2695, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14. 830586 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 1380 of SEQ ID NO:296, b is an integer of 15 to 1394, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater	020567		
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residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14. 830586 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1380 of SEQ ID NO:296, b is an integer of 15 to 1394, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:297, and where bis greater than or equal to a + 14. 830632 Preferably excl	1		AA287593, AA291332, AA492017.
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NO:296, b is an integer of 15 to 1394, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. 830632 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. R8798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646,	, 		
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residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the position of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Restriction of the position of a-b, Restriction of a b, Restrictio			
greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. Branch Alexandrian and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal t			A1089939
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26464, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062707, AA063390, AA062771, AA081934, AA1565278, AA194655, AA470430, AA493634, AA5522261, AA5522348, AA565278, AA566462, AA583788, AA593646.			
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80832, H82603, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552261, AA5522348, AA565462, AA583788, AA593646.	020620		
sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552261, AA5522348, AA565462, AA583788, AA593646.	830632		
where a is any integer between 1 to 984 of SEQ ID NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. H25037, H25038, H25842, H26215, H26994, H28312, H28313, H29756, H30178, H41920, H41966, H42490, H43473, R83733, R85464, R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			R22112, R31393, R32890, R48823,
NO:297, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. H26515, H26994, H28312, H28313, H29756, H30178, H41920, H41966, H42490, H43473, R83733, R85464, R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA156557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			R48824, R66656, R67377, R71682,
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. H29756, H30178, H41920, H41966, H42490, H43473, R83733, R85464, R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			H25037, H25038, H25842, H26215,
residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. H42490, H43473, R83733, R85464, R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			H26515, H26994, H28312, H28313,
residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14. H42490, H43473, R83733, R85464, R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.		and b correspond to the positions of nucleotide	H29756, H30178, H41920, H41966,
greater than or equal to a + 14. R88798, R89058, R93321, H52733, H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.		residues shown in SEQ ID NO:297, and where b is	
H59363, H60020, H73314, H73513, H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.		greater than or equal to a + 14.	R88798, R89058, R93321, H52733
H80831, H80832, H82603, H86794, H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.	•	·	H59363, H60020, H73314, H73513
H86795, H86853, H86852, H92710, H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			H80831, H80832, H82603, H86794
H96832, H98741, N23451, N23463, N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.	•		
N26478, N26861, N31350, N31593, N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			H96832 H98741 N22461 N22462
N35529, N39970, N42652, N62104, N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
N74283, N76446, N78334, N92771, W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
W04383, W19424, W20392, W24569, W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
W35168, W60060, W60111, W84373, W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			µ1/4203, N/0440, N/8334, N927/1,
W84420, AA025658, AA029558, AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
AA062705, AA062707, AA063390, AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
AA062771, AA081934, AA126557, AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
AA136019, AA151638, AA192245, AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
AA194655, AA470430, AA493634, AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			AA136019, AA151638, AA192245,
AA552261, AA552348, AA565278, AA565462, AA583788, AA593646.			
AA565462, AA583788, AA593646.			AA552261, AA552348, AA565278.
AA594277, AA604853, AA613755			
			AA594277, AA604853, AA613755,

830645	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1652 of SEQ ID NO:298, b is an integer of 15 to 1666, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:298, and where b is greater than or equal to a + 14.	AA632449, AA632505, AA657974, AA730677, AA730804, AA748100, AA765824, AA857805, AA954102, AA961763, AA962500, AA974525, AA983564, AA987422, AA987934, AA989423, A1000235, F19140, N84058, N84994, C03222, AA091370, AA091545
830652	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2430 of SEQ ID NO:299, b is an integer of 15 to 2444, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:299, and where b is greater than or equal to a + 14.	·
830659	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1012 of SEQ ID NO:300, b is an integer of 15 to 1026, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:300, and where b is greater than or equal to a + 14.	T65101, T66494, T66636, T84051. T86086, R05580, R13805. R15868, R16050, H05221, H05222. H13512, H16069, H18275, H21247, H44169, R83705, R92365, H48479, H48643, H54436, H54526, H73472. H73726, H97495, N29822, N30479, N31551, N32563, N39176, N39961. N45251, N68667, N91684, W07693. W32510, W32607, W38017, W74179, W79849, AA018138, AA028191, AA033572, AA033571, AA042915, AA043002, AA053878, AA054501, AA058344, AA099556, AA101993, AA134643, AA143525, AA176419, AA424269, AA555196, AA769107, AA987653, A1076212, N84624, N85006, A1084132, A1084154, AA094327
830696	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 816 of SEQ ID NO:301, b is an integer of 15 to 830, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:301, and where b is greater than or equal to a + 14.	
830706	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3286 of SEQ ID NO:302, b is an integer of 15 to 3300, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:302, and where b is	·

	greater than or equal to a + 14.	1
830743	Preferably excluded from the present invention are	N30323, N56655, N69079, N69946.
	one or more polynucleotides comprising a nucleotide	N80244, N98327, W07371, W42660,
	sequence described by the general formula of a-b.	
		W45185, W55989, W56279, W68387,
	where a is any integer between 1 to 461 of SEQ ID	W68503, W72685, W74708, W74677,
	NO:303, b is an integer of 15 to 475, where both a	W77791, W80647, AA010723.
1	and b correspond to the positions of nucleotide	AA011171, AA033537, AA034221,
	residues shown in SEQ ID NO:303, and where b is	AA035773, AA056334, AA062820,
	greater than or equal to a + 14.	AA132021, AA132124, AA135594,
l		AA135681, AA151293, AA151292,
•		AA181331, AA186392, AA187084,
ł		AA228662, AA228680, AA229819,
		AA468802, AA470869, AA483684,
		AA491891, AA514852, AA533423,
	·	AA548946, AA563674, AA564612,
1		AA594511, AA600707, AA622053,
		AA635767, AA639353, AA662887,
l		AA664589, AA729365, AA747035.
		AA747774, AA814124, AA873167,
		AA886626, AA903495, AA903981,
		AA922807, AA969768, AA973174,
		AA974282, AA976458, AA977143,
1		AA983332, AI025140, AI066527,
		F19035, F19464, C03984, C13986,
		C14221, C14299, C14336, C14341,
		C14380, C14385, C14396, C14434,
		C14483, C14504, C14513, C15788
830770	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
]	where a is any integer between 1 to 2888 of SEQ ID	
	NO:304, b is an integer of 15 to 2902, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:304, and where b is	
	greater than or equal to a + 14.	
830830	Preferably excluded from the present invention are	
Ì	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
]	where a is any integer between 1 to 1539 of SEQ ID	
	NO:305, b is an integer of 15 to 1553, where both a	
ĺ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:305, and where b is	
	greater than or equal to a + 14.	
830838	Preferably excluded from the present invention are	
22000	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1973 of SEQ ID	
	NO:306, b is an integer of 15 to 1987, where both a	
	and b correspond to the positions of nucleotide	,
	residues shown in SEQ ID NO:306, and where b is	
2222	greater than or equal to a + 14.	
830851	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 771 of SEQ ID	
	NO:307, b is an integer of 15 to 785, where both a	
	production of the an integer of 15 to 765, where both a	

T46922,
T56001,
R53898,
H77792,
H96065,
N73723,
W03894,
13423,
A143335,
A157208,
A188385,
A501970,
A533759,
A541570,
)4961,
A661481,
A748135,
A885549,
1001062,
N84328,
N85325,
, N86329,
52,
T67857,
H13822,
, AA128266,
A236012,
A987868,
15557
T F

	greater than or equal to a + 14.	
830969	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	•
	where a is any integer between 1 to 502 of SEQ ID	
	NO:313, b is an integer of 15 to 516, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:313, and where b is	
	greater than or equal to a + 14.	į
830991	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1819 of SEQ ID	
ŀ	NO:314, b is an integer of 15 to 1833, where both a	·
	and b correspond to the positions of nucleotide	
l	residues shown in SEQ ID NO:314, and where b is	
	greater than or equal to a + 14.	
831002	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1340 of SEQ ID	
	NO:315, b is an integer of 15 to 1354, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:315, and where b is	
	greater than or equal to a + 14.	
831003	Preferably excluded from the present invention are	T64373, N48387, W52748, W52754,
[31003	one or more polynucleotides comprising a nucleotide	W70187, AA029541, AA034463,
	sequence described by the general formula of a-b,	AA058497, AA082001, AA082284,
	where a is any integer between 1 to 2407 of SEQ ID	AA085967, AA088397, AA133444.
	NO:316, b is an integer of 15 to 2421, where both a	AA133477, AA149568, AA187408,
	and b correspond to the positions of nucleotide	AA226818, AA226855
	residues shown in SEQ ID NO:316, and where b is	111220010, 111220099
	greater than or equal to $a + 14$.	
831021	Preferably excluded from the present invention are	
031021	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1078 of SEQ ID	
	NO:317, b is an integer of 15 to 1092, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:317, and where b is	
	greater than or equal to a + 14.	
831036	Preferably excluded from the present invention are	
021030	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
[where a is any integer between 1 to 1366 of SEQ ID	
	NO:318, b is an integer of 15 to 1380, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:318, and where b is	
	greater than or equal to a + 14.	
831071	Preferably excluded from the present invention are	
7,016	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2598 of SEQ ID	1
	NO:319, b is an integer of 15 to 2612, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:319, and where b is	
	greater than or equal to a + 14.	
ــــــــــــــــــــــــــــــــــــ	Eleator than or equal to a + 14.	

831094	Des Combination of Compiler	
031094	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 929 of SEQ ID	
	NO:320, b is an integer of 15 to 943, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:320, and where b is	
921000	greater than or equal to a + 14.	T50120 T00056 T00150 T01404
831099	Preferably excluded from the present invention are	T58120, T90056, T90158, T94290.
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	R76031, H65424, H65425, N32273,
	where a is any integer between 1 to 2945 of SEQ ID	N40465, N47619, N48504, N66482,
	NO:321, b is an integer of 15 to 2959, where both a	N67212, N67243, N67881, N71915,
	and b correspond to the positions of nucleotide	N72302, N92538, N94512, W03004,
	residues shown in SEQ ID NO:321, and where b is	W06930, W20370, W23962, W38380,
	greater than or equal to a + 14.	W38525, W38716, W39486, W42582,
		W42594, W44824, W48665, W51898,
		W52474, W53040, W60142, N90075,
	1	N90423, AA025009, AA024962.
		AA029382, AA029726, AA031500,
		AA031546, AA037283, AA037749, AA039259, AA044145, AA044261,
		AA065061, AA070027, AA082386,
		AA083544, AA083757, AA088692,
		AA088829, AA099577, AA100236,
		AA100245, AA100517, AA112739,
		AA112091, AA116055, AA130509,
		AA130510, AA132145, AA135909,
		AA136308, AA136413, AA136528,
		AA136751, AA146853, AA146852,
		AA148049, AA156943, AA159808,
	Ì	AA165022, AA173867, AA181803,
		AA182563, AA182776, AA186553,
		AA186858, AA192463, AA194658,
		AA255837, AA261995, AA423999,
	1	AA493599, AA228337, AA228348.
		AA506755, AA506420, AA513968,
		AA514542, AA522900, AA524125,
		AA551485, AA553912, AA563900,
		AA594966, AA602651, AA610339,
	·	AA610361, AA614772, AA618333,
		AA576828, AA665045, AA714493,
		AA729997, AA738153, AA768641,
		AA804931, AA806122, AA827914,
		AA857664, AA876216, AA877173,
		AA877646, AA894385, AA922728,
		AA947835, AA977110, AA984009,
		AA988275, AA988567, N84005,
		N84600, N84939, N85553, A1084028,
		N86141, N88049, N89450, N89451,
		C02877, C02980, C03631, C05243,
		C05332, C05993, AA642453,
		AA090838, AA089614, AA091652,
		AA093130, AA093851
31113	Preferably excluded from the present invention are	AA122085, AA147371, A1005336
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	

	1 200 605010	
İ	where a is any integer between 1 to 788 of SEQ ID	
1	NO:322. b is an integer of 15 to 802, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:322, and where b is	
	greater than or equal to a + 14.	<u> </u>
831120	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1710 of SEQ ID	
	NO:323, b is an integer of 15 to 1724, where both a	
	and b correspond to the positions of nucleotide	
•	residues shown in SEQ ID NO:323, and where b is	
	greater than or equal to a + 14.	
831172	Preferably excluded from the present invention are	
ļ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
l	where a is any integer between 1 to 2247 of SEQ ID	
	NO:324, b is an integer of 15 to 2261, where both a	
ŀ	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:324, and where b is	·
	greater than or equal to a + 14.	
831178	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1199 of SEQ ID	
	NO:325, b is an integer of 15 to 1213, where both a	
İ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:325, and where b is	
	greater than or equal to a + 14.	
831184	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	,
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 2750 of SEQ ID	·
ļ	NO:326, b is an integer of 15 to 2764, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:326, and where b is	•
	greater than or equal to a + 14.	
831203	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1750 of SEQ ID	
	NO:327, b is an integer of 15 to 1764, where both a	
	and b correspond to the positions of nucleotide	
}	residues shown in SEQ ID NO:327, and where b is	
	greater than or equal to a + 14.	1 1 0 5 7 0 1 4 1 0 5 0 7 0 0
831210	Preferably excluded from the present invention are	AA057014, AA059289
}	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	}
	where a is any integer between 1 to 557 of SEQ ID	
	NO:328, b is an integer of 15 to 571, where both a	
]	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:328, and where b is	
	greater than or equal to a + 14.	
831228	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 459 of SEQ ID	

	NO:329, b is an integer of 15 to 473, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:329, and where b is greater than or equal to a + 14.	
831256	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1321 of SEQ ID NO:330, b is an integer of 15 to 1335, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:330, and where b is greater than or equal to a + 14.	R17500. R48877, H12160. R84358, H90367, N33987, AA161057
831257	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID NO:331, b is an integer of 15 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:331, and where b is greater than or equal to a + 14.	T49922, T85470, R37545, H03610, AA005184, AA045346
831277	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1297 of SEQ ID NO:332, b is an integer of 15 to 1311, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:332, and where b is greater than or equal to a + 14.	
831317	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1430 of SEQ ID NO:333, b is an integer of 15 to 1444, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:333, and where b is greater than or equal to a + 14.	T39850, T47708, T47709, T47863, T51491, T52507, T53819, T53951, T55884, T60330, T60359, T60364, T60380, T60480, T60634, T61198, T61280, T61878, T62028, T67704, T67742, T67780, T67853, T67910, T68010, T68058, T68132, T68154, T68379, T68998, T68999, T69078, T69079, T69119, T69177, T69442, T70496, T71707, T72285, T72505, T72998, T73123, T73679, T73756, T73761, T73837, T74031, T74383, T74405, T74655, T74784, T74798, T74892, T85320, T85533, R83453, R88738, R90989, R90995, H58528, H59441, H60092, H60282, H60589, H67401, H67458, H72811, H79422, H80518, H80570, H91775, H91816, N57814, W60714, W60741, AA034367, AA040550, AA040667, AA242768, AA424551, AA424642, R29495, R29660, R29089, C21224
831339	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1016 of SEQ ID NO:334, b is an integer of 15 to 1030, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:334, and where b is	

	greater than or equal to a + 14.	
831363	Preferably excluded from the present invention are	T58736, T58803. T61766. T64470,
	one or more polynucleotides comprising a nucleotide	T64610, T67816, T68878, T68952.
	sequence described by the general formula of a-b.	T72450, T72511, T72968, T73613,
	where a is any integer between 1 to 2113 of SEQ ID	T73939, H41914, H41957, N75040,
•	NO:335, b is an integer of 15 to 2127, where both a	W05718, AA043436, AA043416,
	and b correspond to the positions of nucleotide	AA045231. AA058807, AA484773,
	residues shown in SEQ ID NO:335, and where b is	AA502762, AA503811, AA527553.
	greater than or equal to $a + 14$.	AA744171, AA902935, AA903099,
	greater than or equal to a 7-14.	A1002033
831367	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	•
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 833 of SEQ ID	
	NO:336, b is an integer of 15 to 847, where both a	•
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:336, and where b is	
	greater than or equal to a + 14.	
831379	Preferably excluded from the present invention are	R26001, R26804, R82629, R82630.
	one or more polynucleotides comprising a nucleotide	H21598, H27310, H27309, H38082,
	sequence described by the general formula of a-b,	H38083, H44451, H44494, H47613,
	where a is any integer between 1 to 688 of SEQ ID	R83356, R83791, R96066, R96103,
	NO:337, b is an integer of 15 to 702, where both a	H72512, H72910, H80449, H80450,
	and b correspond to the positions of nucleotide	H90511, H90607, N71766, N94349,
	residues shown in SEQ ID NO:337, and where b is	W16956, W23496, W24351, W46455,
	greater than or equal to a + 14.	W46523, W48658, W70263, W73002,
		W76239, W92963, W92964,
		AA157329, AA157426, AA458665,
		AA229554, AA280810, AA280936,
		AA490898, AA491084, AA493730,
	· -	AA527336, AA534762, AA535794,
	•	F17720, AA603439, AA568655,
		AA659071, AA826699, AA872867,
•	•	AA876999, AA932403, AA953149,
		AA953343, A1000023, A1017353,
		AI094807, N95548, C02063, C04109
831385	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	i
	where a is any integer between 1 to 861 of SEQ ID	
	NO:338, b is an integer of 15 to 875, where both a	
	and b correspond to the positions of nucleotide	}
	residues shown in SEQ ID NO:338, and where b is	
	greater than or equal to a + 14.	1
831390	Preferably excluded from the present invention are	T53890, T54037, T81546, T81973,
	one or more polynucleotides comprising a nucleotide	R20470, R21066, R45288, R46246,
	sequence described by the general formula of a-b,	R45288, R46246, H13340, H17537,
	where a is any integer between 1 to 1434 of SEQ ID	H30523, R85229, R85230, R94643,
	NO:339, b is an integer of 15 to 1448, where both a	R94685, R94686, H52010, H52125,
	and b correspond to the positions of nucleotide	H71328, H71376, N25973, N28794,
	residues shown in SEQ ID NO:339, and where b is	N30891, N36603, N41703, N62205,
	greater than or equal to a + 14.	N63213, N76503, W45706, W44353,
	greater than or equal to a + 14.	W52126, W74523, W79862,
		AA033566, AA034468, AA099015,
		AA099092, AA100315, AA129588, AA167137, AA194961, AA226935,
	•	14 A 16 / 13 / A A 194061 A A 226025
		AA226943, AA418898, AA428909,

831391	Preferably excluded from the present invention are	AA485083. AA485195, AA505107, AA506087. AA516109. AA525370, AA617946. AA627402. AA573848, AA574063, AA809830, AA834509. AA837985, AA862394. AA862989, AA974789. AA988779, A1000171. A1094917, W24010, N88026. C20972
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 829 of SEQ ID NO:340, b is an integer of 15 to 843, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:340, and where b is greater than or equal to a + 14.	
831405	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1279 of SEQ ID NO:341, b is an integer of 15 to 1293, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:341, and where b is greater than or equal to a + 14.	T54632, T54714, T55384, T55812, T56220, T60613, T69578, R08164, R08219, T78003, T78164, R01577. R12676, R16414, H60551, N21984, N25878, N25887, N75352, W01648, W72541, W76166, W86984, W86811, W88909, W88788, AA022691. AA022784, AA193302, AA194256, AA235873, AA425660, AA573463, AA953249, R29055
831442	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1259 of SEQ ID NO:342, b is an integer of 15 to 1273, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:342, and where b is greater than or equal to a + 14.	
831476 ·	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1779 of SEQ ID NO:343, b is an integer of 15 to 1793, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:343, and where b is greater than or equal to a + 14.	R48303, R48405, R73778, H30456, H81254, W02773, W24831, W73089, W73194, AA034015, AA151153, AA151154, AA418429, AA424672, AA593592, AA910532, AA987246, A1001017, C02335, C04320
831488	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1658 of SEQ ID NO:344, b is an integer of 15 to 1672, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:344, and where b is greater than or equal to a + 14.	
831518	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2095 of SEQ ID NO:345, b is an integer of 15 to 2109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:345, and where b is greater than or equal to a + 14.	

831519	Preferably excluded from the present invention are	
Į	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	1
1.	where a is any integer between 1 to 1700 of SEQ ID	
	NO:346, b is an integer of 15 to 1714, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:346, and where b is	
	greater than or equal to a + 14.	
831521	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
1		
	where a is any integer between 1 to 1658 of SEQ ID	
1	NO:347, b is an integer of 15 to 1672, where both a	
	and b correspond to the positions of nucleotide	
1.	residues shown in SEQ ID NO:347, and where b is	
	greater than or equal to a + 14.	
831550	Preferably excluded from the present invention are	
i	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	İ
1	where a is any integer between 1 to 1469 of SEQ ID	
	NO:348, b is an integer of 15 to 1483, where both a	[
	and b correspond to the positions of nucleotide	
ļ	residues shown in SEQ ID NO:348, and where b is	
_	greater than or equal to $a + 14$.	
831560	Preferably excluded from the present invention are	T56429 D22052 D46062 D52265
051500	one or more polynucleotides comprising a nucleotide	T56438, R22852, R46063, R52365,
		R81781, R81879, H02958, H04256,
1	sequence described by the general formula of a-b,	H05743, H05849, H23235, H23349,
l	where a is any integer between 1 to 1828 of SEQ ID	H43210, H43260, H87699, H91571,
	NO:349, b is an integer of 15 to 1842, where both a	W00708, W56717, W56762, W70251,
	and b correspond to the positions of nucleotide	W70252, AA026841, AA027043,
	residues shown in SEQ ID NO:349, and where b is	AA041261, AA041495, AA043451,
ļ	greater than or equal to a + 14.	AA043452, AA054505, AA054366,
		AA055050, AA055129, AA147629,
		AA147667
831562	Preferably excluded from the present invention are	
l	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2994 of SEQ ID	
	NO:350, b is an integer of 15 to 3008, where both a	į
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:350, and where b is	·
	greater than or equal to $a + 14$.	
831570	Preferably excluded from the present invention are	
031370	,	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	ļ
	where a is any integer between 1 to 2742 of SEQ ID	
	NO:351, b is an integer of 15 to 2756, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:351, and where b is	
	greater than or equal to a + 14.	
831593	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	ł
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1631 of SEQ ID	1
	NO:352, b is an integer of 15 to 1645, where both a	İ
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:352, and where b is	·
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	Instantantian or aqual to a ± 14	T T
021506	greater than or equal to a + 14.	
831596	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1623 of SEQ ID	
	NO:353, b is an integer of 15 to 1637, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:353, and where b is	
031607	greater than or equal to a + 14.	A A 147579 A A 156440 A A 599706
831627	Preferably excluded from the present invention are	AA147578, AA156449. AA588796, AA863066. D80116
	one or more polynucleotides comprising a nucleotide	AA803000, D80110
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1105 of SEQ ID	
, '	NO:354, b is an integer of 15 to 1119, where both a	
	and b correspond to the positions of nucleotide	
•	residues shown in SEQ ID NO:354, and where b is	
031640	greater than or equal to a + 14.	R21047
831649	Preferably excluded from the present invention are	121047
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b, where a is any integer between 1 to 724 of SEQ ID	
	NO:355, b is an integer of 15 to 738, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:355, and where b is	
021664	greater than or equal to a + 14.	R35205, H13039, R84255, W24589,
831664	Preferably excluded from the present invention are	W93157, AA186436, AA188774,
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	AA227246, AA658889, AA838204,
	where a is any integer between 1 to 1952 of SEQ ID	W22056, W25833, W28198, W28494,
	NO:356, b is an integer of 15 to 1966, where both a	AA090436, AA089530, AA089667
'	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:356, and where b is	
001604	greater than or equal to a + 14.	
831674	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1548 of SEQ ID	·
	NO:357, b is an integer of 15 to 1562, where both a	İ
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:357, and where b is	
831684	greater than or equal to a + 14. Preferably excluded from the present invention are	T64083, R54664, R54665, W52888,
031084	one or more polynucleotides comprising a nucleotide	W60096, W60162, AA009843,
	sequence described by the general formula of a-b,	AA009870, AA236225, AA236291,
	where a is any integer between 1 to 1917 of SEQ ID	AA459452, AA465675, AA554776,
	NO:358, b is an integer of 15 to 1931, where both a	AA563899, AA583755, AA593849,
	and b correspond to the positions of nucleotide	AA596013, AA627978, AA573921,
	residues shown in SEQ ID NO:358, and where b is	AA747840, AA828086, AA830260,
	greater than or equal to a + 14.	AA837593, AA996154, C01662
021607	Preferably excluded from the present invention are	T49489, R05976, R55046, N21648,
831687	one or more polynucleotides comprising a nucleotide	N31054, N48001, AA464953,
1	sequence described by the general formula of a-b,	AA426224, AA430556, AA600829,
	sequence described by the general formula of a-b,	AA744708. AA747361, AA976473.
	where a is any integer between 1 to 855 of SEQ ID	A1097658
	NO:359, b is an integer of 15 to 869, where both a	M1031030
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:359, and where b is	
1	greater than or equal to a + 14.	<u> </u>

		•
831726 831736	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 547 of SEQ ID NO:360, b is an integer of 15 to 561, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:360, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	T60384, T93026, T83297, R17403,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1666 of SEQ ID NO:361, b is an integer of 15 to 1680, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:361, and where b is greater than or equal to a + 14.	R17423, R21319, H65765, N94506, W23956, W24344, W45068, W57786, W57860, W81343, AA058929, AA151788, AA151833
831762	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 726 of SEQ ID NO:362, b is an integer of 15 to 740, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:362, and where b is greater than or equal to a + 14.	
831801	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1310 of SEQ ID NO:363, b is an integer of 15 to 1324, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:363, and where b is greater than or equal to a + 14.	T39530, T64430, R36089, H12597, H12647, H19534, H20096, H26648, H26663, W15192, W45569, W45621, AA018144, AA018145, AA018470, AA039510, AA039529, AA047549, AA047837, AA057785, AA074201, AA075686, AA079138, AA135599, AA135658, AA147502, AA147931, AA156715, AA156811, AA188215, AA186362, AA425996, AA283917, AA514670, AA522463, AA714301, AA742700, AA872728, AA887841, AA971644, AI015637, AI053971, AI054233, AI074507, AI084901, W28363
831848	sequence described by the general formula of a-b, where a is any integer between 1 to 2839 of SEQ ID NO:364, b is an integer of 15 to 2853, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:364, and where b is greater than or equal to a + 14.	T77112, R13655, R19353, R19511, R24780, R35812, R36752, R38177, R43861, R44629, R45511, R43861, R45511, R44629, R71248, R71299, R82784, H00629, H01917, H04479, H45706, H45757, H94039, H94125, N30574, N57220, AA033684, AA114107, AA253260, AA461547, AA460619, AA715125, AI096588, C03714, AA092127
831861	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1823 of SEQ ID NO:365, b is an integer of 15 to 1837, where both a	T57456, T58038, T58104, R08156, R27046, R28341, R28340, N32411, N56831, N78961, W16984, W16954, W17352, W74522, W79861, AA025882, AA025883, AA084109, AA100121, AA100060, AA132713

831866	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 1809 of SEQ ID	
1	NO:366, b is an integer of 15 to 1823, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:366, and where b is	
	greater than or equal to a + 14.	
831878	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 884 of SEQ ID	
}	NO:367, b is an integer of 15 to 898, where both a	
	and b correspond to the positions of nucleotide	1
1	residues shown in SEQ ID NO:367, and where b is	
	greater than or equal to a + 14.	i ·
831899	Preferably excluded from the present invention are	AA159048, AA768390, AA806956
	one or more polynucleotides comprising a nucleotide	1
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 1103 of SEQ ID	·
	NO:368, b is an integer of 15 to 1117, where both a	
	and b correspond to the positions of nucleotide	
<u> </u>	residues shown in SEQ ID NO:368, and where b is	
	greater than or equal to a + 14.	
831913	Preferably excluded from the present invention are	
131713	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2212 of SEQ ID	
l	NO:369, b is an integer of 15 to 2226, where both a	
1	and b correspond to the positions of nucleotide	:
	residues shown in SEQ ID NO:369, and where b is	`
	greater than or equal to a + 14.	
831972	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3622 of SEQ ID	
	NO:370, b is an integer of 15 to 3636, where both a	·
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:370, and where b is	
	greater than or equal to a + 14.	
831985	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
*	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 4025 of SEQ ID	
	NO:371, b is an integer of 15 to 4039, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:371, and where b is	
	greater than or equal to a + 14.	
831986	Preferably excluded from the present invention are	
031700	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 1585 of SEQ ID	
	NO:372, b is an integer of 15 to 1599, where both a	
	and b correspond to the positions of nucleotide	·
	residues shown in SEQ ID NO:372, and where b is	
	greater than or equal to a + 14.	
832010	Preferably excluded from the present invention are	
032010	i reservoiry excluded from the present invention are	

832016	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 450 of SEQ ID NO:373. b is an integer of 15 to 464, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:373, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 876 of SEQ ID NO:374, b is an integer of 15 to 890, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:374, and where b is greater than or equal to a + 14.	
832041	Preferably excluded from the present invention are	R63637, R92994, N30838, N30844, N41366, N41372. AA639771
832044	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2004 of SEQ ID NO:376, b is an integer of 15 to 2018, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:376, and where b is greater than or equal to a + 14.	T56668, R09616, R20197, R44983, R52998, R52997, R44983, H06485, H06543, H09799, H09885, H24790, N57987, N62197, N76494, W02915, W78217, AA041290, AA041323, AA074236, AA075127, AA075212, AA075847, AA088708, AA088793, AA112359, AA121803, AA151677, AA166711, AA167069, AA181608, AA188478, AA194067, AA194182, AA221025, AA221037, AA228036, AA228145, AA557397, AA564567, AA582681, AA582151, AA601549, AA613841, AA832393, AA846987, AA865356, AA866164, AA872667, AA862962, AA911092, AA937359, A1000072, D83877
832049	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 804 of SEQ ID NO:377, b is an integer of 15 to 818, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:377, and where b is greater than or equal to a + 14.	
832122 832148	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2551 of SEQ ID NO:378, b is an integer of 15 to 2565, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:378, and where b is greater than or equal to a + 14.	T78202, R37864. R62706, R78737,

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1666 of SEQ ID NO:379, b is an integer of 15 to 1680, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:379, and where b is greater than or equal to a + 14.	R78736. H62109, N50394, N51659, N67973, N80394, W33108, W33107. AA016055, AA074831. AA075097, AA256793, AA256472, AA418825, AA4188922. AA430755, AA280663. AA281049, AA467867, AA502148, H71558, AA721278, AA748880, AA809767, AA810852, AA832174, AA911263, AA938484, AA975282, D80672, D81573, D81746, A1096900, C02375
832197	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1253 of SEQ ID NO:380, b is an integer of 15 to 1267, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:380, and where b is greater than or equal to a + 14.	
832237	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1017 of SEQ ID NO:381, b is an integer of 15 to 1031, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:381, and where b is greater than or equal to a + 14.	R36943, R42259, R53230, R42259, H09607, AA150724, AA831055
832246	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1583 of SEQ 1D NO:382, b is an integer of 15 to 1597, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:382, and where b is greater than or equal to a + 14.	H13698, H13750, R91283, R91322, H97506, N64810, N75659, W61290, W65386, H54890, AA568261, AA830860, AA863239, AA873329, AA938701, D82264, C18047
832256	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 161 of SEQ ID NO:383, b is an integer of 15 to 175, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:383, and where b is greater than or equal to a + 14.	
832280	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between I to 2157 of SEQ ID NO:384, b is an integer of 15 to 2171, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:384, and where b is greater than or equal to a + 14.	H09977, H09978, R89392, R94438, H93033, H93466, H93904, N29334, N53767, N57027, N71868, N71879, N73126, W24652, AA026682, AA047124, AA127259, AA224396, AA224473, AA227220, AA236734, AA236763, AA236910, AA236919
832285	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2350 of SEQ ID NO:385, b is an integer of 15 to 2364, where both a	R12740, R14184, R15171, R26447, R28455, R34165, R35396, R39792, R40473, R49696, R41588, R40473, R49696, R70668, R70669, R79640, R79833, H02312, H08199, H08297, R99351, H84241, H84567, H85554,

	residues shown in SEQ ID NO:385, and where b is greater than or equal to a + 14.	N24354, N25230, N32462, N33863, N64676, N70374, N80109, W47526, W47527, W80678, W80934, W93668, AA082195, AA223758, AA243624, AA255527, AA256711, AA262387, AA281015, AA281094, AA281183, AA281203, AA287927, AA287991, AA505084, AA505086, AA525301, AA553559, AA564243, AA582189, AA737010, AA808271, AA872481, AA937541, A1015987, C01015, C20842
832294	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2850 of SEQ ID NO:386, b is an integer of 15 to 2864, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:386, and where b is greater than or equal to a + 14.	
832326	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2669 of SEQ ID NO:387, b is an integer of 15 to 2683, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:387, and where b is greater than or equal to a + 14.	
832333	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1432 of SEQ ID NO:388, b is an integer of 15 to 1446, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:388, and where b is greater than or equal to a + 14.	
832346	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 709 of SEQ ID NO:389, b is an integer of 15 to 723, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:389, and where b is greater than or equal to a + 14.	T88928, R12446, R37113, R42462, H15692, H18859, N34664, AA132220, AA224337, AA460720, AA492479
832370	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID NO:390, b is an integer of 15 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:390, and where b is greater than or equal to a + 14.	
832381	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 685 of SEQ ID NO:391, b is an integer of 15 to 699, where both a	

	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:391, and where b is	
ļ	greater than or equal to a + 14.	
832394	Preferably excluded from the present invention are	,
-	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
}	where a is any integer between 1 to 1531 of SEQ ID	1
	NO:392, b is an integer of 15 to 1545, where both a	
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:392, and where b is	
	greater than or equal to a + 14.	
832454	Preferably excluded from the present invention are	T57094, T58711, T68990, T71879,
	one or more polynucleotides comprising a nucleotide	R92183, H93778, N63977, N80768,
	sequence described by the general formula of a-b,	AA034382, AA034383, AA057664,
	where a is any integer between 1 to 735 of SEQ ID	AA235744, AA425865, AA524693,
	NO:393, b is an integer of 15 to 749, where both a	AA551804, AA523604, AA614639,
	and b correspond to the positions of nucleotide	AA740316, AA872373, AA938571,
	residues shown in SEQ ID NO:393, and where b is	AA947337, R28997, AA640968.
	greater than or equal to a + 14.	C21135
832465	Preferably excluded from the present invention are	R36004, R36378, H71881, H96279,
052.05	one or more polynucleotides comprising a nucleotide	N50049, N63692, W74426, W79180,
	sequence described by the general formula of a-b,	W87805, AA421015, AA527679,
	where a is any integer between 1 to 597 of SEQ ID	AA833773, AA987375, F19351,
	NO:394, b is an integer of 15 to 611, where both a	AA642491, C14893, C14937
	and b correspond to the positions of nucleotide	717042491, 014893, 014937
ł	residues shown in SEQ ID NO:394, and where b is	1
1	greater than or equal to a + 14.	
832475	Preferably excluded from the present invention are	
032473	one or more polynucleotides comprising a nucleotide	
l	sequence described by the general formula of a-b,	
1		
	where a is any integer between 1 to 1842 of SEQ ID	
	NO:395, b is an integer of 15 to 1856, where both a	
	and b correspond to the positions of nucleotide	
Ì	residues shown in SEQ ID NO:395, and where b is	
022405	greater than or equal to a + 14.	
832495	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2637 of SEQ ID	
	NO:396, b is an integer of 15 to 2651, where both a]
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:396, and where b is	
222 455	greater than or equal to a + 14.	
832498	Preferably excluded from the present invention are	Γ67126, T67127, R13516, R20638,
		H64071, N22361, N25516, N39506,
		N75609, N78204, W40313, W45344,
	where a is any integer between 1 to 2493 of SEQ ID	AA074739, AA074803, AA143509,
	NO:397, b is an integer of 15 to 2507, where both a	AA523999, AA552542, AA554032,
	and b correspond to the positions of nucleotide	N20483, AA588804, AA617733,
	residues shown in SEQ ID NO:397, and where b is	AA577150, AA577309, AA579423,
	greater than or equal to a + 14.	AA740813, AA835721, AA836640,
		AA909766, AA936979, AA947310,
		N26815. A1085484, D78707, W67520.
		W68152
832501	Preferably excluded from the present invention are	
ひろとうひし	preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	

	where a is any integer between 1 to 1259 of SEQ ID	
ł	NO:398, b is an integer of 15 to 1273, where both a	
ł	and b correspond to the positions of nucleotide	1
1	residues shown in SEQ ID NO:398, and where b is	
	greater than or equal to a + 14.	
832505	Preferably excluded from the present invention are	T50501, T50636, T92136, R52390.
į	one or more polynucleotides comprising a nucleotide	R59648. H06170, H28886, H28885,
	sequence described by the general formula of a-b,	R96577, R96600, H84171, H94122,
	where a is any integer between 1 to 3760 of SEQ ID	H98228, N36866, N36872, N46136,
	NO:399, b is an integer of 15 to 3774, where both a	N46142, N63589, N66323, W48779.
	and b correspond to the positions of nucleotide	W49798. AA029033, AA054487,
	residues shown in SEQ ID NO:399, and where b is	AA058524, AA084466, AA086177,
i	greater than or equal to a + 14.	AA098967, AA099485, AA100345,
		AA147008, AA147009, AA146910,
		AA146909, AA160346, AA159865,
1		AA192832, AA203513, AA252521,
	ļ.	AA252553, AA463513, AA463570,
		AA421250, AA425704, AA427774,
		AA278328, AA278999, AA280712,
		AA281733, AA281871, AA282407,
	ţ	AA282626, AA283639, AA542810,
		AA557893, AA568486, AA569759,
		AA577522, AA659517, AA659737,
		AA664537, AA713950, AA805488,
1	·	AA835999, AA876619, AA931568,
		AA935758, AA946722, A1000603,
		D82640
832539	Preferably excluded from the present invention are	H72563, AA160114, AA159654,
	one or more polynucleotides comprising a nucleotide	AA161261, AA165097, AA223618,
	sequence described by the general formula of a-b,	AA243203
	where a is any integer between 1 to 1508 of SEQ ID	
	NO:400, b is an integer of 15 to 1522, where both a	
l	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:400, and where b is	
1	greater than or equal to a + 14.	
832554	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
l	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1356 of SEQ ID	
	NO:401, b is an integer of 15 to 1370, where both a	· .
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:401, and where b is	
L	greater than or equal to a + 14.	
832569	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
ŀ	where a is any integer between 1 to 1398 of SEQ ID	
1	NO:402, b is an integer of 15 to 1412, where both a	
[and b correspond to the positions of nucleotide	!
	residues shown in SEQ ID NO:402, and where b is	
L_	greater than or equal to a + 14.	
832578	Preferably excluded from the present invention are	R09545, R09658, R09967, R11471,
	one or more polynucleotides comprising a nucleotide	R16714, R16910, R16965, R19372,
	sequence described by the general formula of a-b,	R80788, R80988, H28725, H63085,
	where a is any integer between 1 to 1736 of SEQ ID	H63169, H75499, H75500, N33554,
	NO:403, b is an integer of 15 to 1750, where both a	N41536, N52961, N52966, N74070,
1	and b correspond to the positions of nucleotide	W01039, W57770, W57843, W60109,

	1 :	W01070 W07107
	residues shown in SEQ ID NO:403, and where b is	W91978, W92107, AA001984,
	greater than or equal to a + 14.	AA004653, AA027155, AA418427,
	·	AA281395, AA532870. AA564737,
		AA588889, AA631841, AA639548,
		AA765363, AA877896, AA887900,
		AA974026, Al057270, Al084214,
		A1094490, A1096750, A1097632,
		A1096745
832615	Preferably excluded from the present invention are	
ĺ	one or more polynucleotides comprising a nucleotide	
Ì	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1325 of SEQ ID	
	NO:404, b is an integer of 15 to 1339, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:404, and where b is	
İ	greater than or equal to a + 14.	
832620	Preferably excluded from the present invention are	· · · · · · · · · · · · · · · · · · ·
	one or more polynucleotides comprising a nucleotide	
•	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 468 of SEQ ID	
l	NO:405, b is an integer of 15 to 482, where both a	
1	and b correspond to the positions of nucleotide	
ļ	residues shown in SEQ ID NO:405, and where b is	
İ	greater than or equal to a + 14.	
832632	Preferably excluded from the present invention are	
032032	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1399 of SEQ ID	
	NO:406, b is an integer of 15 to 1413, where both a	
·		
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:406, and where b is	
022622	greater than or equal to a + 14.	D(0172 A 4052005 A 4052507
832633	Preferably excluded from the present invention are	R69173, AA053085, AA053597,
1	one or more polynucleotides comprising a nucleotide	AA427705, AA730380, AA865757,
	sequence described by the general formula of a-b,	AA911497, AI083906
	where a is any integer between 1 to 1679 of SEQ ID	
}	NO:407, b is an integer of 15 to 1693, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:407, and where b is	
	greater than or equal to a + 14.	
833483	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1328 of SEQ ID	
	NO:408, b is an integer of 15 to 1342, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:408, and where b is	
	greater than or equal to a + 14.	
834574	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2403 of SEQ ID	
	NO:409, b is an integer of 15 to 2417, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:409, and where b is	
	greater than or equal to a + 14.	
	M. J	

1	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
i	where a is any integer between 1 to 1387 of SEQ 1D	
	NO:410, b is an integer of 15 to 1401, where both a	
ł	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:410, and where b is	
	greater than or equal to a + 14.	
834861	Preferably excluded from the present invention are	
ļ	one or more polynucleotides comprising a nucleotide	i .
}	sequence described by the general formula of a-b,	
·	where a is any integer between 1 to 3002 of SEQ ID	
	NO:411, b is an integer of 15 to 3016, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:411, and where b is	
	greater than or equal to a + 14.	· ·
834890	Preferably excluded from the present invention are	T40255, T40256, T40770, T40778,
037070	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	T40803, T41118, T94280, T94627, R13201, R32388, R32389, R53769,
	where a is any integer between 1 to 944 of SEQ ID	
1	NO:412, b is an integer of 15 to 958, where both a	H28669, H39502, H42532, H42533,
		R82957, R85205, R85206, R88749,
,	and b correspond to the positions of nucleotide	R90730, R90754, R91006, R92221,
	residues shown in SEQ ID NO:412, and where b is	H56130, H56210, H58500, H57659,
	greater than or equal to a + 14.	H69479, H69882, N22547, N31579,
•		N42592, N45537, N48687, N56654,
•		N58050, N69059, N73728, N80748,
		N92927, N94545, W20471, W30838,
		W52039, W60171, W68292, W93085,
		W93140, N91563, AA010850,
]		AA011289, AA054592, AA054780,
.		AA081135, AA081214, AA081655,
		AA081936, AA082127, AA082262,
		AA088665, AA088804, AA102560,
		AA100239, AA114237, AA115714,
		AA115715, AA127304, AA127303,
		AA147789, AA148021, AA149821,
		AA152050, AA160878, AA169126,
		AA171659, AA172131, AA172285,
		AA194597, AA243129, AA419357,
	· ·	AA425135, AA426203, AA244212,
	'	AA505963, AA508221, AA527434,
		AA527878, AA565036, F17736,
	·	AA582605, AA582728, AA583851,
		AA586421, AA601920, AA570580,
	,	AA574367, AA577515, AA577538,
		AA565998, AA657417, AA659655,
		AA662658, AA665113, AA714991,
		AA770684, AA808865, AA826971,
		AA838507, AA876809, AA877842,
		AA878025, AA886042, AA886643,
		AA877950, AA937751, AA948428,
		AA947036, AA973473, AA983150,
		AA989361, A1082367, D78922,
		D82096, N83321, C04115, R29685,
		C17110, C18023, C18068, AA093539,
		AA094947, AA151399, AA654145,
		AA654136
925070	Proforably avaluded from the properties and	
835079	Preferably excluded from the present invention are	N25566, W00985, AA081340,

sequence described by the general formula of a-b, where a is any integer between 1 to 486 of SEQ ID NO:413, b is an integer of 15 to 500, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:413, and where b is greater than or equal to a + 14.	AA152231, AA164282, AA171619, AA187113, A1073932
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3383 of SEQ ID NO:414, b is an integer of 15 to 3397, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:414, and where b is greater than or equal to a + 14.	
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2866 of SEQ ID NO:415, b is an integer of 15 to 2880, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:415, and where b is	
Preferably excluded from the present invention arc one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1602 of SEQ ID NO:416, b is an integer of 15 to 1616, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:416, and where b is greater than or equal to a + 14.	T71562, R11480, R19383, R25309, R46659, R48802, R48913, R50038, R50376, R54963, R46659, R70030, R70077, R70161, R71380, R72303, R72352, R72772, R72773, R73386, R73387, H15775, H15776, H25239, H27204, H30499, H42026, H42613, H43207, H43254, H44314, H44936, H44975, R98394, R98395, R99071, R99271, H58902, H58903, H73590, H73436, H75566, H80599, N40440, N48475, N59703, AA515035, AA515043, AA515450, AA515650, AA515746, AA551788, AA551943, AA554602, AA557281, AA581549, AA581554, AA587399, AA593890, AA593997, AA593998, AA568878, AA568962, AA622458, AA714206, AA728962, AA737738, AA738036, AA738486, AA847538, AA865069, AA872029, AA886612, AA903381, AA916458, AA916464, AA922563, AA928617, AA928314, AA934581, AA973769, AA973767, AA983480, AA991199, AA994932, AA995182, AA999704, A1028371, AA643041
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1801 of SEQ ID NO:417, b is an integer of 15 to 1815, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:417, and where b is greater than or equal to a + 14.	2.2.2.03, A1020371, AA043041
	where a is any integer between I to 486 of SEQ ID NO:413, b is an integer of 15 to 500, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:413, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between I to 3383 of SEQ ID NO:414, b is an integer of 15 to 3397, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:414, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between I to 2866 of SEQ ID NO:415, b is an integer of 15 to 2880, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:415, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between I to 1602 of SEQ ID NO:416, b is an integer of 15 to 1616, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:416, and where b is greater than or equal to a + 14.

		
835817	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 1952 of SEQ ID	1
	NO:418. b is an integer of 15 to 1966, where both a	
1	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:418, and where b is	
	greater than or equal to a + 14.]
835840	Preferably excluded from the present invention are	T66583, R15957, R22860, R62339,
055040 .	one or more polynucleotides comprising a nucleotide	R62341, R62856, AA210836,
}	sequence described by the general formula of a-b,	AA214633, AA256340, AA732582,
		1
1	where a is any integer between 1 to 2838 of SEQ ID	AA740735
	NO:419, b is an integer of 15 to 2852, where both a	1
ļ	and b correspond to the positions of nucleotide	
j	residues shown in SEQ ID NO:419, and where b is	<u> </u>
	greater than or equal to a + 14.	
836048	Preferably excluded from the present invention are	<u> </u>
1	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2691 of SEQ ID	
ļ	NO:420, b is an integer of 15 to 2705, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:420, and where b is	<u> </u>
	greater than or equal to a + 14.	
836898	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 1887 of SEQ ID	
ŀ	NO:421, b is an integer of 15 to 1901, where both a	
1	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:421, and where b is	
1	greater than or equal to a + 14.	
836927	Preferably excluded from the present invention are	
030,2.	one or more polynucleotides comprising a nucleotide	
ŀ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2463 of SEQ ID	
	NO:422, b is an integer of 15 to 2477, where both a	
l		
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:422, and where b is	
027244	greater than or equal to a + 14.	
837344	Preferably excluded from the present invention are	
}	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
l	where a is any integer between 1 to 763 of SEQ ID	
İ	NO:423, b is an integer of 15 to 777, where both a	
1	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:423, and where b is	
l	greater than or equal to a + 14.	
837789	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
]	where a is any integer between 1 to 1635 of SEQ ID	
	NO:424, b is an integer of 15 to 1649, where both a	
j	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:424, and where b is	
1	greater than or equal to a + 14.	
838549	Preferably excluded from the present invention are	
		+

one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 420 of SEQ ID NO:430, b is an integer of 15 to 434, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1809 of SEQ ID NO:431, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14.			
sequence described by the general formula of a-b, where a is any integer between 1 to 1594 of SEQ ID NO:425, b is an integer of 15 to 1608, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:425, and where b is greater than or equal to a + 14. 838754 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1780 of SEQ ID NO:426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 t		one or more polynucleotides comprising a nucleotide	
where a is any integer between 1 to 1594 of SEQ ID NO-425, b is an integer of 15 to 1608, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO-425, and where b is greater than or equal to a + 14. 838754			
NO.425, bis an integer of 15 to 1608, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:425, and where b is greater than or equal to a + 14. 838754 838754 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1780 of SEQ ID NO.426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1450 of SEQ ID NO:430, b is an integer of 15 to 140.040 where b is greater than or equal to a + 14. Preferably excluded from the prese	i		
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:425, and where b is greater than or equal to a + 14. 838754 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 1780 of SEQ ID NO:426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 1436 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 1400 of SEQ ID NO:430, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide sequence described by the general formula of a -b, where a is any integer between 1 to 1400 of SEQ ID NO:430, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in	ļ		
residues shown in SEQ ID NO:425, and where b is ereater than or equal to a ± 14. 838754 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1780 of SEQ ID NO:426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:426, and where b is greater than or equal to a ± 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a ± 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a ± 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a ± 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 140 of SEQ ID NO:430, b is an integer of 15 to 143, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a ± 14. 84006			
ereater than or equal to a + 14. 838754 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1780 of SEQ ID NO:426, b is an integer of IS to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of IS to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is areater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of IS to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO:429, b is an integer of IS to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 180 of SEQ ID NO:430, b is an integer of IS to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present inventio			
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1780 of SEQ ID NO:426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1450 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1450 of SEQ ID NO:429, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1400 of SEQ ID NO:430, b is an integer of 15 to 1434, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. Preferably excluded from t			ļ .
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1780 of SEQ ID NO.426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO.427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO.428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO.429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO.430, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general	838754		
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where a is any integer between 1 to 1780 of SEQ ID NO.426, b is an integer of 15 to 1794, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.426, and where b is greater than or equal to a + 14. 838768 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO.427, b is an integer of 15 to 770. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO.428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.428, and where b is greater than or equal to a + 14. 839561 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO.429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO.429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO.430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO.430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO.431, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one			
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residues shown in SEQ ID NO:426, and where b is greater than or equal to a + 14. 838768 Préferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a + 14. 839486 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. 839961 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1456 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a + 14. 839816 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. 840068 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1809 of SEQ ID NO	1		
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Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO:427, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:427, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:428, b is an integer of 15 to \$12, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:428, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 145 of SEQ ID NO:429, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:429, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1420 of SEQ ID NO:430, b is an integer of 15 to 1470, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:430, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general			
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Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1809 of SEQ ID NO:431, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are		greater than or equal to a + 14.	
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1809 of SEQ ID NO:431, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. 840279 Preferably excluded from the present invention are	840068		
sequence described by the general formula of a-b, where a is any integer between 1 to 1809 of SEQ ID NO:431, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. 840279 Preferably excluded from the present invention are		one or more polynucleotides comprising a nucleotide	
where a is any integer between 1 to 1809 of SEQ ID NO:431, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. 840279 Preferably excluded from the present invention are		sequence described by the general formula of a-b,	
NO:431, b is an integer of 15 to 1823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are		where a is any integer between 1 to 1809 of SEQ ID	
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. 840279 Preferably excluded from the present invention are		NO:431, b is an integer of 15 to 1823, where both a	1
residues shown in SEQ ID NO:431, and where b is greater than or equal to a + 14. 840279 Preferably excluded from the present invention are			1
greater than or equal to a + 14. 840279 Preferably excluded from the present invention are			
840279 Preferably excluded from the present invention are		greater than or equal to a + 14.	
one or more polynucleotides comprising a nucleotide	840279	Preferably excluded from the present invention are	
		one or more polynucleotides comprising a nucleotide	

		1
1	sequence described by the general formula of a-b,	
ł	where a is any integer between 1 to 3377 of SEQ ID	
. ·	NO:432, b is an integer of 15 to 3391, where both a	·
	and b correspond to the positions of nucleotide	
•	residues shown in SEQ ID NO:432, and where b is	
	greater than or equal to a + 14.	
840489	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	į
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2539 of SEQ ID	
1	NO:433, b is an integer of 15 to 2553, where both a	
	and b correspond to the positions of nucleotide	
İ	residues shown in SEQ ID NO:433, and where b is	
	greater than or equal to a + 14.	
840538	Preferably excluded from the present invention are	T47551, T47552, T64522, T65947,
	one or more polynucleotides comprising a nucleotide	R70190, H97064, N25641, N34240,
	sequence described by the general formula of a-b,	N48063, N53261, N67904, N92702,
	where a is any integer between 1 to 2518 of SEQ ID	N98774, W16899, W20316, W31028,
ļ	NO:434, b is an integer of 15 to 2532, where both a	W40137, W45371, W48722, W48577,
1	and b correspond to the positions of nucleotide	W68670, W68773, W74242,
	residues shown in SEQ ID NO:434, and where b is	AA033573, AA033574, AA063270,
1	greater than or equal to a + 14.	AA063271, AA065213, AA064894,
		AA082200, AA083707, AA085441,
ł	,	AA085694, AA088302, AA088303,
ł]	AA099844, AA099984, AA102604,
1		AA111894, AA112981, AA115039,
1	ł	AA115800, AA115799, AA122221,
		AA126905, AA126955, AA127109,
1 .		AA127548, AA127549, AA128933,
l		AA129152, AA129743, AA133290,
1		AA135251, AA151963, AA156321,
1		AA156382, AA160182, AA165104,
	, in the second	AA164688, AA173757, AA180038,
1		AA182644, AA190866, AA190959,
Ì		AA191561, AA191637, AA197348,
		AA195895, AA258593, AA258622,
		AA262173, AA464978, AA465047,
	,	AA417938, AA418116, AA292727,
]		AA523585, AA525020, AA548516,
	· ·	AA551816, AA554642, AA581720,
1		AA568802, AA579801, AA738216,
į		AA832441, AA903391, AA938688,
		AA977201, AA987552, A1095102,
		A1084149, W27768, C05889, C06263,
1		AA089556, AA652586, AA213999,
1		AA213977, AA219123, AA219290,
1		AA435695, D12383, D12389,
Ī		AA451677, AA453222, AA485641,
		AA485768, AA488670, AA485947,
1		AA486053, AA486197, AA489511,
		AA489512, AA489558, AA491452,
1		AA489876, AA600130, AA608644,
		AA620481, AA664307, AA629754,
}		AA629909, AA677148, AA722910,
l	1	AA772440, AA773550, Al038219,
1	1	A1075755, A1081932, A1084706,
i		T10852, T24678, F00208, F00897

<u> </u>		
840545	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	· ·
	where a is any integer between 1 to 1808 of SEQ ID	
	NO:435, b is an integer of 15 to 1822, where both a	
	and b correspond to the positions of nucleotide	•
	residues shown in SEQ ID NO:435, and where b is	
	greater than or equal to a + 14.	
840549	Preferably excluded from the present invention are	R10733, T86298, R55182, R55183,
	one or more polynucleotides comprising a nucleotide	H00476, H00530, H25856, H25909,
	sequence described by the general formula of a-b,	H25910, N50923, W84600, W84452,
	where a is any integer between 1 to 1016 of SEQ ID	AA227897, D78774, AA486440,
	NO:436, b is an integer of 15 to 1030, where both a	AA629249
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:436, and where b is	
	greater than or equal to a + 14.	
840551	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1618 of SEQ ID	
	NO:437, b is an integer of 15 to 1632, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:437, and where b is	
	greater than or equal to a + 14.	
840557	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1002 of SEQ ID	
	NO:438, b is an integer of 15 to 1016, where both a	
•	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:438, and where b is	
	greater than or equal to a + 14.	
840561	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	_
:	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 580 of SEQ ID	
	NO:439, b is an integer of 15 to 594, where both a	1
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:439, and where b is	
	greater than or equal to a + 14.	
840562	Preferably excluded from the present invention are	R08937, R09046, R14796, R18307,
	one or more polynucleotides comprising a nucleotide	R31150, R42283, R51828, R54224,
	sequence described by the general formula of a-b,	R42283, R72104. R72156, R73118,
	where a is any integer between 1 to 1566 of SEQ ID	R73171, R73943, H25904, H27191,
	NO:440, b is an integer of 15 to 1580, where both a	H27192, H30471, H72478, H72879,
	and b correspond to the positions of nucleotide	H88214, H98231, W45061, W45071,
	residues shown in SEQ ID NO:440, and where b is	W49842, W67423, W67424, W93880,
	greater than or equal to a + 14.	W94151, AA023007, AA022473,
	·	AA032224, AA032282, AA034411,
		AA035691, AA040428, AA046861,
		AA046994, AA046313, AA046139,
		AA053780, AA101657, AA101658,
	· ·	AA167298. AA227543, AA227684,
		AA458877, AA459067, AA463656,
		AA464047, AA464754, AA225370,
		AA225425, AA225400, AA558796,
	•	AA582089. AA565830, AA713907,

		AA864510, AA936117, C01002,
	}	N86320, C04277, AA652714,
		AA402391, AA402565, AA479073,
		AA621791, AA670200, AA456544,
ļ		AA676732, AA707089, AI014599,
		A1022852, A1023739, A1091873,
		A1094288, Z39517, Z43438
840564	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1068 of SEQ ID	
	NO:441, b is an integer of 15 to 1082, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:441, and where b is	
	greater than or equal to a + 14.	ļ
840572	Preferably excluded from the present invention are	T87514, T87515, H84879, AA001503,
	one or more polynucleotides comprising a nucleotide	AA506411, AA508167, AA715396,
	sequence described by the general formula of a-b,	AA931268, AA292666, AA478036,
	where a is any integer between 1 to 1227 of SEQ ID	AA478193, AA478194, AA707886,
	NO:442, b is an integer of 15 to 1241, where both a	
		AA724969, AA725050, AA779127, AA843885
	and b correspond to the positions of nucleotide	MM043003
	residues shown in SEQ ID NO:442, and where b is greater than or equal to a + 14.	
840600	Preferably excluded from the present invention are	D20172 A A 22/740 A A 40/420
640000 I		R38172, AA226748, AA484320,
	one or more polynucleotides comprising a nucleotide	AA831852
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 954 of SEQ ID	1
	NO:443, b is an integer of 15 to 968, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:443, and where b is	
242624	greater than or equal to a + 14.	
840604	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1346 of SEQ ID	
	NO:444, b is an integer of 15 to 1360, where both a	
	and b correspond to the positions of nucleotide	·
	residues shown in SEQ ID NO:444, and where b is	
0.40.600	greater than or equal to a + 14.	
840608	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1821 of SEQ ID	
	NO:445, b is an integer of 15 to 1835, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:445, and where b is	
	greater than or equal to a + 14.	
840620	Preferably excluded from the present invention are	R17303, R41982, R41982, H43756,
		N62762, AA053677, AA053697,
		AA084224, AA084019, AA084952,
		AA419123, AA419160, AA426014,
	· · · · · · · · · · · · · · · · · · ·	AA425077, AA427847, AA524035,
	pro.440, o is an integer of 15 to 1555, where both a	
		,
	and b correspond to the positions of nucleotide	AA565019, AA632254, AA745726,
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:446, and where b is	AA565019, AA632254, AA745726, AA835832, AA931712, AA932520,
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:446, and where b is greater than or equal to a + 14.	AA565019, AA632254, AA745726,

<u> </u>		AA488554, AA620470, AA781416.
		AA844227, AI090902, T19161
840625 840626	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 361 of SEQ ID NO:447, b is an integer of 15 to 375, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:447, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1379 of SEQ ID NO:448, b is an integer of 15 to 1393, where both a	AA844227, A1090902, 119161
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:448, and where b is	
840638	greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1649 of SEQ ID NO:449, b is an integer of 15 to 1663, where both a	H01158, H01159, H05751, H05858, H83341, H83695, N47512, N47513, W39756, W79733, W90027, W90155, AA047691, AA047741, AA086374, AA100549, AA159315, AA159414,
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:449, and where b is greater than or equal to a + 14.	AA282525, AA282633, AA595381, AA688093, AA744757, AA865203, AA933811, AA969838, AA975917, F18424, D12197, D12219, AA478596, AA665540, AA909221, AA969720, A1049820
840649	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1366 of SEQ ID NO:450, b is an integer of 15 to 1380, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:450, and where b is greater than or equal to a + 14.	R00133, R22651, R44356, R44356, R56353, R93194, N47106, N50316, N50780, N55139, AA010596, AA010597, AA012940, AA012888, AA013216, AA013313, AA017544, AA017417, AA047814, AA047792, AA235545, AA262268, AA262879, AA563873, AA570239, AA573586, AA827412, AA862337, AA902472, AA962409, AA971292, AA973596, A1056509, A1080455, AA410833, T23822, T16761
840651	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 912 of SEQ ID NO:451, b is an integer of 15 to 926, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:451, and where b is greater than or equal to a + 14.	
840666	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1628 of SEQ ID NO:452, b is an integer of 15 to 1642, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:452, and where b is greater than or equal to a + 14.	N32778, N34353, N34537, N41780, N42818, N93337, W25190, AA035229, AA035230, AA044070, AA044162, AA195074, AA195174, AA419441, AA731906, AA761315, AA761330, AA766382, AA766593, AA769537, AA805515, AA806516, AA809893, AA814954, AA857917, N44554,

		AA393941. A1074651, T10618, Z35722
840681	Preferably excluded from the present invention are	MASSSATI, MINIANSI, 110010, 233/22
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2240 of SEQ ID	
	NO:453, b is an integer of 15 to 2254, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:453, and where b is	
	greater than or equal to a + 14.	
840682	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1917 of SEQ ID	
	NO:454, b is an integer of 15 to 1931, where both a	
	and b correspond to the positions of nucleotide	
	recidues shown in SEO ID NO.454 and where his	·
	residues shown in SEQ ID NO:454, and where b is	
840684	greater than or equal to a + 14.	
D-1004	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
·	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 757 of SEQ ID	
	NO:455, b is an integer of 15 to 771, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:455, and where b is	1
240607	greater than or equal to a + 14.	
340697	Preferably excluded from the present invention are	R00751, R02584, R02703, R69879,
	one or more polynucleotides comprising a nucleotide	R69927, H13156, H29249, H29248,
	sequence described by the general formula of a-b,	H41216, R83398, H54666, H54667,
	where a is any integer between 1 to 1155 of SEQ ID	H73551, H73552, H90468, H91760,
	NO:456, b is an integer of 15 to 1169, where both a	H97869, N31729, N31735, N51232,
	and b correspond to the positions of nucleotide	W32147, W32175, W44313, W45660,
	residues shown in SEQ ID NO:456, and where b is	W57760, W57761, W68386, W68502,
	greater than or equal to a + 14.	W68752, W68835, W72538, W76163,
		AA035740, AA043246, AA043585,
		AA044419, AA043053, AA047593,
		AA047601, AA088798, AA147253,
•		AA155747, AA160105, AA165689,
		AA172386, AA173747, AA189005,
		AA189006, AA471066, AA507210,
		AA513086, AA516406, AA514685,
		AA635861, AA657400, AA668796,
J		AA737126, AA768005, AA768358,
		AA887459, AA977176, D80509,
		D81008, D81471, D81800, D82666,
		N83795, AA643662, AA284937,
		AA290823, AA447984, AA448126,
		AA676807, AA709464, AA780333,
		AA843801, AA853391, AA868403,
		AA917460, T17166, T17177, T16671,
		T48481, T48507
40698	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3235 of SEO ID	
	where a is any integer between 1 to 3235 of SEQ ID NO:457, b is an integer of 15 to 3249, where both a	
	where a is any integer between 1 to 3235 of SEQ ID NO:457, b is an integer of 15 to 3249, where both a and b correspond to the positions of nucleotide	

	greater than or equal to a + 14.	
840708	Preferably excluded from the present invention are	R21272, R45362, R45362, H06049,
	one or more polynucleotides comprising a nucleotide	H13385, AA082768, AA101114,
	sequence described by the general formula of a-b.	AA131634, AA131718, AA152290.
	where a is any integer between 1 to 1902 of SEQ ID	AA150232, AA418083, AA418230,
	NO:458, b is an integer of 15 to 1916, where both a	AA422115, AA424919, AA426139.
	and b correspond to the positions of nucleotide	AA741277, AA749290, AA811505,
	residues shown in SEQ ID NO:458, and where b is	AA836102, AA411231, AA453804,
	greater than or equal to a + 14.	AA453890, AA758905, AA769817,
	Broad Mair or oqual to a 11.	AA770192, AA904708, AA905158,
		AA969156, Al093952, Z42470,
		Z41665, Z44053
840714	Preferably excluded from the present invention are	
•	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2759 of SEQ ID	
	NO:459, b is an integer of 15 to 2773, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:459, and where b is	
	greater than or equal to a + 14.	į
840716	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2017 of SEQ ID	·
	NO:460, b is an integer of 15 to 2031, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:460, and where b is	
	greater than or equal to a + 14.	1
840721	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1825 of SEQ ID	
	NO:461, b is an integer of 15 to 1839, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:461, and where b is	
	greater than or equal to a + 14.	
840735	Preferably excluded from the present invention are	T47277, T56085, T93319, T85388,
	one or more polynucleotides comprising a nucleotide	H57620, H58465, N77902, N80219,
	sequence described by the general formula of a-b,	N93978, W19715, W37380, W37643,
	where a is any integer between 1 to 765 of SEQ ID	W38508, W38722, W47048, W68079,
	NO:462, b is an integer of 15 to 779, where both a	W67976, W69349, W69350,
	and b correspond to the positions of nucleotide	AA025313, AA024560, AA063371,
	residues shown in SEQ ID NO:462, and where b is	AA063370, AA463222, AA463223,
	greater than or equal to a + 14.	AA424422, AA469264, AA480510,
	•	AA507733, AA524348, AA557233,
		AA602394, AA603318, AA631014,
		AA569554, AA575944, AA688112,
		AA911131, AA932225, AA937015,
		AA994856, AI077707, N92552,
		W00604, C00184, AA292823,
		AA401683, AA663906, AA664122,
		AA771943, AA779608, AA812529,
		A1028120, A1027559, A1032511,
	Ì	AI033880, AI034204, AI078458,
		AI041685, D31473, T64469
840738	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	

]	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 1703 of SEQ ID	
1	NO:463, b is an integer of 15 to 1717, where both a	
1	and b correspond to the positions of nucleotide	
,	residues shown in SEQ ID NO:463, and where b is	
	greater than or equal to a + 14.	
840745	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 814 of SEQ ID	
	NO:464, b is an integer of 15 to 828, where both a	
1	and b correspond to the positions of nucleotide	
ł	residues shown in SEQ ID NO:464, and where b is	
	greater than or equal to a + 14.	1
840747	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1159 of SEQ ID	
	NO:465, b is an integer of 15 to 1173, where both a	
	and b correspond to the positions of nucleotide	
l	residues shown in SEQ ID NO:465, and where b is	·
] .	greater than or equal to a + 14.	•
840756	Preferably excluded from the present invention are	AA074254
	one or more polynucleotides comprising a nucleotide	[
	sequence described by the general formula of a-b,	1
	where a is any integer between 1 to 507 of SEQ 1D	
	NO:466, b is an integer of 15 to 521, where both a	į
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:466, and where b is	
	greater than or equal to a + 14.	
840776	Preferably excluded from the present invention are	T47069, T47068, T63511, T63587,
1	one or more polynucleotides comprising a nucleotide	T79637, T79722, R36141, R36419,
	sequence described by the general formula of a-b,	R65831, R65934, R69612, R69701,
<u> </u>	where a is any integer between 1 to 1414 of SEQ ID	H00464, H00514, H04572, H04575,
ŀ	NO:467, b is an integer of 15 to 1428, where both a	H12602, H12652, H13166, H66218,
	and b correspond to the positions of nucleotide	H67195, H67868, H67868, N62959,
	residues shown in SEQ ID NO:467, and where b is	W92249, W92250, W92609, W95234,
	greater than or equal to $a + 14$.	
	greater than of equal to a + 14.	AA007598, AA193373, AA195360, AA195359, AA425046, AA430627,
		AA428172, AA484871, AA557201,
		AA902998, AA927360, N79862,
		AA479674, AA477192, AA481418,
		AA481651, AA495983, AA496377,
		AA496655, AA912146, AA912181,
040704	Draforchly avaluded from the second	AI049805, AA693485
840784	Preferably excluded from the present invention are	·
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3449 of SEQ ID	
	NO:468, b is an integer of 15 to 3463, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:468, and where b is	•
	greater than or equal to a + 14.	
840788	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 607 of SEQ ID	

	NO:469, b is an integer of 15 to 621, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:469, and where b is	
	greater than or equal to a + 14.	
840794	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1819 of SEQ ID	
	NO:470, b is an integer of 15 to 1833, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:470, and where b is	
	greater than or equal to a + 14.	
840797	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3188 of SEQ ID	
	NO:471, b is an integer of 15 to 3202, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:471, and where b is	İ
ļ	greater than or equal to a + 14.	
840799	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 927 of SEQ ID	
	NO:472, b is an integer of 15 to 941, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:472, and where b is	
	greater than or equal to a + 14.	·
840818	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1265 of SEQ ID	
	NO:473, b is an integer of 15 to 1279, where both a	
	and b correspond to the positions of nucleotide	·
i	residues shown in SEQ ID NO:473, and where b is	
l	greater than or equal to a + 14.	
840822	Preferably excluded from the present invention are	T47621, T77305, T83423, R18484,
	one or more polynucleotides comprising a nucleotide	R51973, R51974, R73192, H06082,
	sequence described by the general formula of a-b,	H12940, H27135, H45895, H45904,
	where a is any integer between 1 to 3195 of SEQ ID	N72089, W00342, W52213, W96404,
	NO:474, b is an integer of 15 to 3209, where both a	AA045488, AA058907, AA062768,
	and b correspond to the positions of nucleotide	AA069032, AA081439, AA082427,
	residues shown in SEQ ID NO:474, and where b is	AA084417, AA101216, AA234022,
Ì	greater than or equal to a + 14.	AA534011, AA565390, AA588319,
		AA588430, AA568701, AA635907,
		AA579930, AA827039, AA857519,
	· ·	AA872490, AA904077, AA995057,
		AI073336, N95359, C15883,
		AA781445, AA906492, AI037943,
		A1039428
840830	Preferably excluded from the present invention are	N33920, N33932, N49642, N49629,
1	one or more polynucleotides comprising a nucleotide	AA508747, AA514767, AA583465.
	sequence described by the general formula of a-b,	AA805203, AA878968, U37231,
]	where a is any integer between 1 to 819 of SEQ ID	Т24573
l	NO:475, b is an integer of 15 to 833, where both a	
	and b correspond to the positions of nucleotide	
L	residues shown in SEQ ID NO:475, and where b is	<u> </u>

	greater than or equal to a + 14.	
840846	Preferably excluded from the present invention are	T68706, T68719, T68771, T68784,
•	one or more polynucleotides comprising a nucleotide	T73424, T73431, T73486, T73492,
	sequence described by the general formula of a-b,	T73499, T73535, T89865, R11465,
	where a is any integer between I to 1127 of SEQ ID	T79345, T79774, T81799, T82119,
	NO:476. b is an integer of 15 to 1141, where both a	T82855, T96198, T96454, T96686,
	and b correspond to the positions of nucleotide	T96802, T96920, T97027, T99996,
	residues shown in SEQ ID NO:476, and where b is	T99997, R00156, R00157, R83404,
	greater than or equal to $a + 14$.	R85816, R91357, R93314, R94713,
	Scores diam of oqual to a * 1 is	R94794, R97348, R99024, R99798,
		H48280, H48369, H48754, H54738,
	1	H54739, H55985, H55984, H56050,
		H56244, H57662, H57872, H57873,
		H58502, H60170, H60211, H62933,
		H69203, H69228, H69229, H71630,
	•	H73011, H73012, H81193, H81194,
	ł	H90826, H91385, N33963, N49672,
		N49822, N52577, N54836, N58435,
	1	N64440, N66934, N69249, N69373,
		N74062, N75759, N78025, N78145,
		N94249, N95116, W03303, W01169,
		W01912, N91401, AA025243,
		AA026028, AA193126, AA194255,
		AA236507, AA242995, AA622239,
	+	AA575858, AA575872, AA576026,
		AA576150, AA576597, AA864932,
		AA877934, AA969761, AA994970,
	į	A1017867, D82634, C21067,
		AA431221, AA779655, AA782374,
		AA812640, AA923315, AA962377,
		AA993251, AI018445, AI025584,
340848	D-C-11	A1092470, T79311
940040	Preferably excluded from the present invention are	R10066, R10163, T26606, R61067,
	one or more polynucleotides comprising a nucleotide	R72646, H08322, H47858, H47859,
	sequence described by the general formula of a-b,	R86048, H68866, H68867, H69098,
	where a is any integer between 1 to 1088 of SEQ ID	H82364, N58491, N78080, W52876,
	NO:477, b is an integer of 15 to 1102, where both a	W60083, AA043086, AA045865,
	and b correspond to the positions of nucleotide	AA045866, AA055712, AA057298,
	residues shown in SEQ ID NO:477, and where b is	AA058743, AA079887, AA079888,
	greater than or equal to a + 14.	AA099233, AA099234, AA102153,
		AA113213, AA115932, AA121000,
		AA131067, AA143412, AA146598,
		AA155632, AA155688, AA160447,
		AA173257, AA173248, AA195987,
	·	AA196375, AA233537, AA463552,
		AA503072, AA551794, AA586410,
		AA594814, AA613123, AA573356,
		AA580449, AA731195, AA742856,
		AA827930, AA863440, AA865529,
		AA876847, AA953614, AA976924,
		N84278, N88762, C17112, AA219765,
		AA284503, AA293437, AA293046,
		AA669435, AA722103, A1027785,
		A1073617, A1092707, T17392, F08770,
		D12026
40860	Preferably excluded from the present invention are	T89645, T89919, T93704, R21871,
		R22387, R78094, R78181, R78515,

sequence described by the general formula of a-b, R78560, H40124, H41731, N28359, where a is any integer between 1 to 4187 of SEQ ID N42893, N62851, N64787, N67463, NO:478, b is an integer of 15 to 4201, where both a N76199, N77065, N77758, W67341, and b correspond to the positions of nucleotide W68381, AA034244, AA044935, residues shown in SEQ ID NO:478, and where b is AA045056, AA057392, AA057684, greater than or equal to a + 14. AA071214, AA071442, AA081937, AA082360, AA082229, AA082230, AA082708, AA083297, AA083188, AA127585, AA149575, AA151791, AA167113, AA173360, AA191227, AA195437, AA223329, AA223614, AA243268, AA261939, AA262815, AA262816, AA422160, AA426276, AA225924, AA504466, AA504634, AA522823, AA554566, AA632813, AA576873, AA662886, AA730326, AA748669, AA828942, AA837197, AA857065, AA857683, AA862276, AA864246, AA873317, A1083733, D82604, D82635, N81179, N85023, N85166, N85712, C00193, C00199, C02425, N87331, N88683, N88852, N89408, C02916, C05151, C06382, AA642209, C21319, AA091285, AA091688, AA094300, AA205974, AA206268, AA206598, AA205324, AA649340, AA247212, AA404505, AA421263, AA421361, D11545, AA441853, AA441826, AA463350, AA463858, AA487271, AA487388, AA496439, AA496488, AA634627, AA663685, AA665466, AA456144, AA722996, AA772136, AA772153, AA774179, AA992418, AI076734, T10506, Z30218, Z38961, T16262, T48571, D31110, D45597, F06042, F00682 840861 Preferably excluded from the present invention are T52180, T52256, T57048, T60934, one or more polynucleotides comprising a nucleotide T60993, T94137, T94228, T91060, sequence described by the general formula of a-b, T85924, R23216, R23292, R31316, where a is any integer between 1 to 773 of SEQ ID R31576, R62640, R62693, H03198, NO:479, b is an integer of 15 to 787, where both a H18231, H18269, H22414, H26112, and b correspond to the positions of nucleotide H26116, H26378, H40754, H38895, residues shown in SEQ ID NO:479, and where b is H47721, H48072, R89134, R89141, greater than or equal to a + 14. R91829, R91836, R98452, H65626, H65627, H69728, H71913, H71914, H78844, H80090, H83062, H84585, H87467, H87577, H93457, H93458, N23179, N30549, N32644, N39052, N40455, N48060, N48244, N53258, N53755, N63557, N94559, N94883, N94981, N95791, N42987, W19445, W19573, W23831, W24902, W30850, W32700, W32701, W37523, W56867, W60497, W60972, W61219, W69268, W69346, W80426, W80556, W94817, W95832, W95966, W96035, W96092,

	·	N90310, AA010147, AA010148,
1		AA025440. AA025757, AA027347,
1		AA027822, AA027874, AA029650,
l		AA029651. AA037779, AA039260,
	'	AA046801. AA046818, AA054707.
		AA058654, AA062684, AA063287,
1		AA074876, AA074979, AA084381,
1		
		AA085264. AA085328, AA085598,
		AA122190. AA120978, AA133892,
l		AA129630, AA172403, AA172206,
1		AA190489, AA190525, AA464455,
ĺ		AA464996, AA225769, AA259210,
		AA483109, AA483741, AA493542,
		AA502162, AA516183, AA522567,
		AA526813, AA557654, AA588882,
		AA593799, AA576216, AA659530,
		AA662308, AA688246, AA688254,
	·	AA687457, AA687516, AA689236,
		AA728852, AA729032, AA747479,
		AA747979, AA831447, AA887348,
		AA903105, AA916516, AA934714,
		AA953363, AA976759, AA991410,
ĺ		AA991434, AI002147, AI028033,
ł		N83338, C02469, R29174, AA090669,
		AA092066, AA648634, AA443968,
		AA444149, AA482243, AA482340,
		AA485406, AA598458, AA644566,
		AA664032, AA680199, AA676482,
		AA629708, AA630110, AA457100,
1		AA431269, AA405296, AA405332,
		AA721997, AA724146, AA774657,
		AA781529, AA781641, AA781838,
,		AA782849, AA813171, AA843229,
		AA846744, AA846814, AA854299,
		AA854765, AA789029, AA993047,
		AI023973, AI027725, AI031943,
	·	A1038463, A1041602, A1085085,
		A1086504, A1088189
840871	Preferably excluded from the present invention are	H42821, AA028094, AA099211,
	•	AA160368, AA223572, AA232552,
	sequence described by the general formula of a-b,	AA252811
	where a is any integer between 1 to 717 of SEO ID	MAZ32011
	NO:480, b is an integer of 15 to 731, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:480, and where b is	
040074	greater than or equal to a + 14.	
840874	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1105 of SEQ ID	
	NO:481, b is an integer of 15 to 1119, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:481, and where b is	
	greater than or equal to a + 14.	
840878	Preferably excluded from the present invention are	T40405, T41252, T47240, T47241,
840878	one or more polynucleotides comprising a nucleotide	T40405, T41252, T47240, T47241, T50233, T52891, T57110, T58359, R19508, R43858, R43858, R75598,

	where a is any integer between 1 to 2042 of SEQ ID	R75665, H13192, H13193, N25264,
	NO:482, b is an integer of 15 to 2056, where both a	N31900. N42683, N72995, N93388.
İ	and b correspond to the positions of nucleotide	W25360, W47628, W47629,
	residues shown in SEQ ID NO:482, and where b is	AA009691, AA009410, AA045777,
1	greater than or equal to a + 14.	AA045910, AA063040, AA063076,
·	T '	AA130044, AA149205, AA149206,
i		AA191678, AA252698. AA464304,
1		AA225264, AA514845, AA526726,
		AA548411, AA548704, AA552050,
	·	AA552558, AA568675, AA827017,
	·	AA834447, AA838450. AA886357.
		AA886653, AA887879. AA916602,
Į.		
İ		AA928685, AA968793, A1005016,
1		W28859, AA134038, AA455118,
		AA496380, AA496656, AA598830,
1		AA653270, AA725217, AA733068,
1		A1004394, A1023815, A1026954,
\$40880	Des Countries and and Countries and and and and and and and and and and	A1040891. Z25388, Z28470, AA702322
040080	Preferably excluded from the present invention are	H02306, H02418, N48196, N53344,
}	one or more polynucleotides comprising a nucleotide	AA059013, AA506159, AA613938,
,	sequence described by the general formula of a-b,	AA662759, AA976725, AA854631
	where a is any integer between 1 to 873 of SEQ ID	
	NO:483, b is an integer of 15 to 887, where both a	· .
	and b correspond to the positions of nucleotide	
l	residues shown in SEQ ID NO:483, and where b is	
<u> </u>	greater than or equal to a + 14.	·
840884	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	1
1	sequence described by the general formula of a-b,	1
	where a is any integer between 1 to 1864 of SEQ ID	
	NO:484, b is an integer of 15 to 1878, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:484, and where b is	
Ĺ	greater than or equal to a + 14.	·
840907	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	<u> </u>
l	sequence described by the general formula of a-b,	į
1	where a is any integer between 1 to 1552 of SEQ ID	
	NO:485, b is an integer of 15 to 1566, where both a	
	and b correspond to the positions of nucleotide	
!	residues shown in SEQ ID NO:485, and where b is	
	greater than or equal to a + 14.	
840926	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	[
	where a is any integer between 1 to 3032 of SEQ ID	
	NO:486, b is an integer of 15 to 3046, where both a	İ
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:486, and where b is	
	greater than or equal to $a + 14$.]
840932	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1890 of SEQ ID	
1	NO:487, b is an integer of 15 to 1904, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:487, and where b is	
L	residues shown in SEQ 1D 110.401, and whele 0 is	L

	greater than or equal to a + 14.	
840940	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
	where a is any integer between 1 to 813 of SEQ ID	
	NO:488, b is an integer of 15 to 827, where both a	
	and b correspond to the positions of nucleotide	
•	residues shown in SEQ ID NO:488, and where b is	
	greater than or equal to a + 14.	
840947	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1912 of SEQ ID	· ·
	NO:489, b is an integer of 15 to 1926, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:489, and where b is	
	greater than or equal to a + 14.	
840959	Preferably excluded from the present invention are	
040737	one or more polynucleotides comprising a nucleotide	,
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1447 of SEQ ID	
	NO:490, b is an integer of 15 to 1461, where both a	
	and b correspond to the positions of nucleotide	·
	residues shown in SEQ ID NO:490, and where b is	
	greater than or equal to a + 14.	•
840964	Preferably excluded from the present invention are	R79226, H12332, H51062, H83364,
040704	one or more polynucleotides comprising a nucleotide	H89523, N27508, N30527, N40233,
	sequence described by the general formula of a-b,	N52503, N53855, N94367, AA055215,
	where a is any integer between 1 to 791 of SEQ ID	AA055306, AA188169, AA468498,
	NO:491, b is an integer of 15 to 805, where both a	AA470473, AA563662, AA622643,
	and b correspond to the positions of nucleotide	AA579613, AA668790, AA748160,
	residues shown in SEQ ID NO:491, and where b is	AA765447, AA873430, AA879079,
•	greater than or equal to $a + 14$.	AA903275, AA970424, N73354,
ļ	greater than or equal to a + 14.	AA402259, AA883758, AA890505,
		AA906005, AI023931
840979	Preferably excluded from the present invention are	111500003,711023531
040777	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2255 of SEQ ID	
	NO:492, b is an integer of 15 to 2269, where both a	
İ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:492, and where b is	
	greater than or equal to a + 14.	
840984	Preferably excluded from the present invention are	
D-10204	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 4094 of SEQ ID	
	NO:493, b is an integer of 15 to 4108, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:493, and where b is	1
	greater than or equal to $a + 14$.	
840986	Preferably excluded from the present invention are	H25393, H25394, H25511, H25512,
040780	one or more polynucleotides comprising a nucleotide	R95750, R95794, H64076, H64131,
	sequence described by the general formula of a-b,	H68715, H80548, H80604, H94681,
		H95039, H99481, N28293, N30167,
	where a is any integer between 1 to 2195 of SEQ ID	N35782, W47389, W47262, W61304,
1	NO:494, b is an integer of 15 to 2209, where both a	
	and b correspond to the positions of nucleotide	W65368, AA054346, AA054383,

	residues shown in SEO ID NO-404 and and and and	A A O S P 2 2 0 A A O S P 4 4 0 A A S P 2 0 5 1
	residues shown in SEQ ID NO:494, and where b is	AA058320, AA058448, AA512954.
İ	greater than or equal to a + 14.	AA558416, AA588459, AA935690.
j		A1097565, N87339, AA993027.
		AA993568, AA701454, AA702350
840988	Preferably excluded from the present invention are	T87048, R24473, R43337, R43337.
	one or more polynucleotides comprising a nucleotide	N75007, W05750, AA182467.
	sequence described by the general formula of a-b.	AA227466, AA504464, AA504538.
ļ	where a is any integer between 1 to 1663 of SEQ ID	AA923479, AA648887, AA663889.
	NO:495, b is an integer of 15 to 1677, where both a	A1027636, A1028506, A1026720.
	and b correspond to the positions of nucleotide	Z42717
l	residues shown in SEQ ID NO:495, and where b is	
	greater than or equal to a + 14.	
840990	Preferably excluded from the present invention are	
ĺ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1688 of SEQ ID	
	NO:496, b is an integer of 15 to 1702, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:496, and where b is	
	greater than or equal to a + 14.	
840992	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2362 of SEQ ID	
	NO:497, b is an integer of 15 to 2376, where both a	
	and b correspond to the positions of nucleotide	
i	residues shown in SEQ ID NO:497, and where b is	
	greater than or equal to $a + 14$.	'
841009	Preferably excluded from the present invention are	T40224 T41105 T70150 T70221
0 11 007		T40334, T41195, T79150, T79231,
	one or more polynucleotides comprising a nucleotide	T85615, T98895, T99485, R25796,
1	sequence described by the general formula of a-b,	H03311, H03312, H11314, H21245,
	where a is any integer between 1 to 826 of SEQ ID	R91754, R91755, R93025, R97834,
	NO:498, b is an integer of 15 to 840, where both a	R97886, R99577, R99583, R99683,
	and b correspond to the positions of nucleotide	R99689, H88057, H97799, H97870,
	residues shown in SEQ ID NO:498, and where b is	N34019, N35363, N42786, N44738,
	greater than or equal to a + 14.	N52502, N70158, N72884, N74746,
		N93542, N95357, N98354, W01181,
		W03108, W15165, W19587, W21350,
		W24700, W24805, W39226, W48682,
		W49637, W49739, W51977, W67546,
		W67528, W67665, W79731, W93828,
		W93829, AA025348, AA025356,
		AA024401, AA024402, AA029589,
		AA029588, AA099331, AA099865,
		AA121627, AA126717, AA126816,
		AA126817, AA133155, AA165162,
		AA165163, AA557332, AA640015,
		AA579505, AA665011, AA665221,
	İ	AA738009, AA830748, AA918150,
		AA918992, AA947223, AA974955,
		A1083731, N56157, N89240,
		MANOONO AANOANA AACCONO
		AA092060, AA094384, AA650291,
		AA292814, AA402491, F20671,
		F21115, D11655, D11564, D11605,
		D12048, AA634049, U54738,
		AA732766, AA782030, AA843638,
		AA860477, AA861482, A1018649,

		A1092171, Z28714, T23956, AA694568
841012	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 447 of SEQ ID NO:499, b is an integer of 15 to 461, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:499, and where b is greater than or equal to a + 14.	
841016	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2768 of SEQ ID NO:500, b is an integer of 15 to 2782, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:500, and where b is greater than or equal to a + 14.	R21854. R21868. R23349, R27518, R63726, R63775, R65731, R65957, R65958, R66192, R66977, R66978, R67072, R69600, R69690, H12415, H12416, N46541, N47260, N47778, N48572. N51984. N95008, W25613, W31713, W32142, W38029, W38650, W38655, AA037660, AA039268, AA042908, AA042921. AA063533, AA126558, AA130121, AA130157, AA137270, AA136020, AA232954, AA233044, AA429346, AA429872, AA565520, AA604780, AA610435, AA631349, AA631518, AA740206, AA770618, AA912228, A1079705, N84191, N85956, N92894, W38030, C00380, N83173, C03262, AA092010, U82782, AA247592, AA284977, AA283619, AA291890, AA293636, AA410312, AA410537, AA453566, AA487623, AA626442, AA628932, AA629190, AA629753, AA629916, AA719528, AA843073, AA844228, AA890492, A1024670, A1051881, A1061324, F11149
841017	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1235 of SEQ ID NO:501, b is an integer of 15 to 1249, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:501, and where b is greater than or equal to a + 14.	R21764, R21815, N71125, W17312, AA112660, AA179538, AA179507, AA902202, AA907419, AA913594, AA994481, AI049652
841021	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1344 of SEQ ID NO:502, b is an integer of 15 to 1358, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:502, and where b is greater than or equal to a + 14.	R23836, W38704, AA033686, AA176734, AA192268, AA525913, AA531505, AA532666, AA533781, AA533827, AA533949, AA554396, AA576754, AA906883, N24273, C14272, C14285, C14286, C18998
841032	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 487 of SEQ ID NO:503, b is an integer of 15 to 501, where both a and b correspond to the positions of nucleotide	T41136, T52990, T52991, T61494, T63001, T63145, T87321, T87328, T89480, T84361, R05264, N75935, W05120, W25352, AA191627, AA258512, AA418549, AA224774, AA225253, AA229538, AA229537,

		1
	,	AA229951. AA230318, AA468106.
		AA468170. AA482814. AA482855,
		AA482894. AA482906. AA483676,
		AA491563, AA491627, AA492175,
		AA501375, AA502205, AA505498.
		AA508058. AA508125, AA512979,
		AA513165, AA523347, AA528170,
		AA531497, AA542840, AA551430.
		AA553992, AA554420, AA582164.
	•	AA583205. AA593192, AA593362,
		AA602125, AA603378, AA603728,
		AA617691, AA622865, AA630937,
		AA631991. AA570802, AA569520,
	1 • • • • • • • • • • • • • • • • • • •	AA654990, AA664728, AA664864,
		AA665278, AA729616, AA729639,
		AA729652, AA730512, AA730705,
		AA730910, AA737300, AA737303,
		AA736808, AA736909, AA738098,
		AA740165, AA740553, AA742574,
		AA742885, AA746988, AA747057,
		AA747094, AA747099, AA747961,
		AA748108, AA804727, AA805835,
	·	AA834105, AA838466, AA864527,
		AA872303, AA875939, AA876612,
		AA876936, AA879219, AA885735,
		AA886033, AA888159, AA888528,
		AA88683, AA903652, AA935001,
		AA948734, AA947836, AA978250,
		AA994661, AI073926, AI085517,
		N83676, N86451, N87989, AA642538,
		AA090432, AA090481, AA092225,
		AA091643, AA094678, AA094818,
		AA095214, AA648652, AA649783,
	· ·	AA650377, AA401641, F21163,
		AA411822, AA442212, AA609798,
		AA679909, F22052, AA679265,
		AA722456, A1003421, A1028430,
		A1077884, A1086743, T89286, R05321,
		AA694044
841051	Preferably excluded from the present invention are	AA427363
1031	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	sequence described by the general tollida of a-b,	
	where a is any integer between 1 to 1997 of SEQ ID	
	NO:504, b is an integer of 15 to 2011, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:504, and where b is	
	greater than or equal to a + 14.	
841064	Preferably excluded from the present invention are	R95695, H49073, H61707, H61911,
	one or more polynucleotides comprising a nucleotide	H68517, H89719, H89781, H89828,
	sequence described by the general formula of a-b,	H90680, N76870, W88654, W88898,
	where a is any integer between 1 to 1975 of SEQ ID	AA046748, AA053076, AA053592,
	NO:505, b is an integer of 15 to 1989, where both a	AA127256, AA127257, AA187351.
	and b correspond to the positions of nucleotide	AA188218, H67307, AA602545,
}	residues shown in SEQ ID NO:505, and where b is	AA720701, AA742288, N87596,
		AA094084, AA204976, AA676787,
ł	greater than or equal to a + 14.	AA703221, AA779414, Al038609,
1		
		A1074626, A1088527, T17364,

		AA702787
841069	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1071 of SEQ ID NO:506. b is an integer of 15 to 1085, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:506, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1471 of SEQ ID NO:507, b is an integer of 15 to 1485, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:507, and where b is greater than or equal to a + 14.	
841078	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1916 of SEQ ID NO:508, b is an integer of 15 to 1930, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:508, and where b is greater than or equal to a + 14.	T39937, T68962, T84426, R20697, R36425, R45643, R45643, R68137, R70943, R70957, R70996, R71011, H02222, H05658, H05659, H25177, H29362, H54732, H54733, H60311, H60310, H77561, H77562, H78245, H78446, H82436, H82699, N20477, N57742, N59418, N59709, N76617, AA029237, AA055009, AA055434, AA236337, AA425703, AA427773, AA482193, AA482287, AA612777, AA729757, AA737276, AA744359, AA872776, AA972581, C06045, AA446583, AA449748, AA707197, AA757691, AA774691, AA992571, A1003756, A1027513, A1039704, A1042272, A1052652, A1077380, A1083949, AA774036
841080	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1120 of SEQ ID NO:509, b is an integer of 15 to 1134, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:509, and where b is greater than or equal to a + 14.	
841088	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1368 of SEQ ID NO:510, b is an integer of 15 to 1382, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:510, and where b is greater than or equal to a + 14.	R00895, R21561, R42090, R42090, H05080, N79589, N94381, W16578, W42724, W42813, W46346, W46347, W47346, W57707, W57783, AA070469, AA490938, AA586820, AA580196, AA745683, AA809239, AA931405, D11601, AA725448, AA992145, A1023735, A1025359, A1031575, A1033697, A1038145, A1093535, F00072
841092	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1727 of SEQ ID	

	NO:511. b is an integer of 15 to 1741, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:511, and where b is	·
	greater than or equal to a + 14.	
841095	Preferably excluded from the present invention are	W20114, AA255840, AA568302.
	one or more polynucleotides comprising a nucleotide	AA406006, AA434170 ·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1516 of SEQ ID	
	NO:512, b is an integer of 15 to 1530, where both a	ļ
	and b correspond to the positions of nucleotide	İ
	residues shown in SEQ ID NO:512, and where b is	
	greater than or equal to a + 14.	
841096	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2985 of SEQ ID	
	NO:513, b is an integer of 15 to 2999, where both a	· '
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:513, and where b is	·
	greater than or equal to a + 14.	
841102	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	1
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2034 of SEQ ID	
	NO:514, b is an integer of 15 to 2048, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:514, and where b is	
	greater than or equal to a + 14.	
841104	Preferably excluded from the present invention are	T93851, R05295, R05354, R71097,
	one or more polynucleotides comprising a nucleotide	R71445, R99396, N53129, W38359,
j	sequence described by the general formula of a-b,	W38417, W38418, W39384, W44785,
	where a is any integer between 1 to 3286 of SEQ ID	W44786, W69719, W69847, W73703,
	NO:515, b is an integer of 15 to 3300, where both a	AA134718, AA164646, AA164647,
	and b correspond to the positions of nucleotide	AA418958, AA420439, AA420440,
	residues shown in SEQ ID NO:515, and where b is	AA548241, AA548224, AA558195,
	greater than or equal to a + 14.	W73847, Z19840, AA707354,
		AA868898, AA917430, AI073454,
		F09131, F11469, AA700476
841108	Preferably excluded from the present invention are	T89709, T89806, T91163, T93774,
	one or more polynucleotides comprising a nucleotide	T93819, T95226, R06420, R06475,
	sequence described by the general formula of a-b,	R23277, R23370, R32742, R32743,
	where a is any integer between 1 to 3411 of SEQ ID	R52354, R52355, R64095, R64184, R65984, R65985, R70225, R70226,
	NO:516, b is an integer of 15 to 3425, where both a	R76344, R76672, R80205, H00679,
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:516, and where b is	H00770, H04254, H24758, H24803, H40273, H38053, H38054, H47116,
	greater than or equal to a + 14.	
1		H47210, R92478, R94873, R94872, H57866, H57867, H59353, H61105,
1		•
		H63261, H63535, H63938, H67759, H67760, H77384, H77385, H82932,
		H87435, H87541, H88753, H88754, N59081, N59489, N63682, N63939,
		N66851, N70709, N92122, N99845,
	·	W32595, W88585, W90769, W90327,
1		W93082, W93137, AA025425,
		AA041232, AA114914, AA114913, AA128525, AA235362, AA235944,
		MA140141, MA411304, MA431744,

841118	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1344 of SEQ ID NO:517, b is an integer of 15 to 1358, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:517, and where b is greater than or equal to a + 14.	AA235945. AA425197, AA636023, AA639557. AA729723. AA907495. A1056355, A1089809, AA448599. AA449742, AA476262, AA478567, AA478700. AA599706, AA634117, AA677126, AA716562, AA923333. AA948589, A1051569, A1073816, A1074666, A1080341, A1084428, A1090962. A1096407 R20815. R36529, R38448, R46586, R46586, R71122, R71625, R77658, R80438. R80643. H12595, H12644, H99733, N20132, N25939, N29738, N57157, N59874, N67154, N67834, W03438, W04625, W31524, AA044199, AA044996, AA135739, AA135782, AA146912, AA146911, AA173589, AA224431, AA232224, AA256600, AA256599, AA419270, AA419321, AA425195, AA484744, AA507823, AA513832, AA584296, AA600955, AA614813, AA807248, AA904059, AA937796, AA973678, AA983325, AA991604, W01284, C16969, AA476260, AA476318,
		AA476367, AA609550, AA678511, AA722726, AA904676, AA954468,
841119	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1354 of SEQ ID NO:518, b is an integer of 15 to 1368, where both a and b correspond to the positions of nucleotide	A1001869, A1031538, Z41297 R18472, W39766, AA076303, AA985235
	residues shown in SEQ ID NO:518, and where b is greater than or equal to a + 14.	
841124	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 919 of SEQ ID NO:519, b is an integer of 15 to 933, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:519, and where b is greater than or equal to a + 14.	·
841137	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1416 of SEQ ID NO:520, b is an integer of 15 to 1430, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:520, and where b is greater than or equal to a + 14.	T65560, R52978, R59392, H24368, H25185, N33308, AA016160, AA019434, AA082036, AA099724, AA099725, AA101466, AA100553, AA100634, AA100635, AA143046, AA150250, AA151129, AA165491, AA172129, AA176104, AA176248, AA176272, AA197310, AA227454, AA232220, AA243156, AA261904, AA262541, AA458854, AA459044, AA481155, AA493247, AA514323, AA522820, AA558368, AA582973, AA604489, AA640528, AA569125,

ſ		AA569824, AA737640, AA743846,
		AA808232, AA812222, AA847813,
		AA865060, AA872242, AA872353,
		AA922866. AA933823, AA988358,
		•
		A1056397. A1085865, A1088865,
		AA205921. AA205923, AA205997,
		AA204887, AA205731, D11887,
		AA634040, AA703823, AA703893,
		Z20424, AA707344, AA707416,
	1	AA716243, AA683201, AA890456,
	,	A1003274, A1076618, A1090177,
		T10877, Z28746, T25145, Z40353,
	•	F11026, F09670, AA699695,
		AA701137
841143	Preferably excluded from the present invention are	T52948, T57468, T59332, T91403,
041143	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	R77675, R77676, H30692, H70576,
	where a is any integer between 1 to 1155 of SEQ ID	N24036, N24905, N26173, N35858,
	NO:521, b is an integer of 15 to 1169, where both a	N36029, W39771, W45303, W80648,
	and b correspond to the positions of nucleotide	W80649, AA029895, AA029983,
	residues shown in SEQ ID NO:521, and where b is	AA036639, AA036850, AA043430,
	greater than or equal to a + 14.	AA043431, AA046109, AA046196,
		AA076106, AA076107, AA083131,
		AA083181, AA083285, AA083293,
		AA147761, AA147804, AA155831,
		AA155741, AA430082, AA581553,
1		AA593886, AA594233, AA604399,
	1	AA576339, AA715836, AA730946,
		AA737298, AA768251, AA872423,
	· ·	AA888276, AA961744, AA962699,
i		AA975874, AI000132, R29417,
ľ		AA640954, AA094702, AA398483,
		AA402600, AA489817, AA489948,
		AA496290, AA663953, AA663986,
		AA725581, AA771972, AA781165,
		AA845829, AA772618, AA773208,
		AA907551, A1003883, A1004593,
		AI031669, AI052123, AI085380
841148	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2148 of SEQ ID	
	NO:522, b is an integer of 15 to 2162, where both a	
		1
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:522, and where b is	1
	greater than or equal to a + 14.	
841149	Preferably excluded from the present invention are	AA812937
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	1
	where a is any integer between 1 to 785 of SEQ ID	
	NO:523, b is an integer of 15 to 799, where both a	·
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:523, and where b is	
	greater than or equal to $a + 14$.	
041151		
841151	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
L	sequence described by the general formula of a-b,	1

		,
	where a is any integer between 1 to 1708 of SEQ ID	
	NO:524. b is an integer of 15 to 1722, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:524, and where b is	
	greater than or equal to a + 14.	
841155	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	ł
	where a is any integer between 1 to 548 of SEQ ID	
l	NO:525, b is an integer of 15 to 562, where both a	
	and b correspond to the positions of nucleotide	·
i .	residues shown in SEQ ID NO:525, and where b is	
	greater than or equal to a + 14.	
841161	Preferably excluded from the present invention are	H81836, AA015599, AA099033,
	one or more polynucleotides comprising a nucleotide	AA099034, AA211818, AA741499,
	sequence described by the general formula of a-b,	AA748367, AA768854, AA805297,
1	where a is any integer between 1 to 2009 of SEQ ID	AA804217, AI000120, AI090415,
	NO:526, b is an integer of 15 to 2023, where both a	D79280, D79875, AA628397,
į	and b correspond to the positions of nucleotide	AA628438, AA889584, Z36757
	residues shown in SEQ ID NO:526, and where b is	
ł	greater than or equal to a + 14.]
841162	Preferably excluded from the present invention are	T54529, T54568, T39916, T40885.
D 11102	one or more polynucleotides comprising a nucleotide	T64421, T64740, T94433, T94519,
.]	sequence described by the general formula of a-b,	T94763, T94764, T67443, T67536,
1	where a is any integer between 1 to 2833 of SEQ ID	T69533, R08782, R08783, T84049,
	NO:527, b is an integer of 15 to 2847, where both a	T86084, R18023, R19657, R33054,
l	and b correspond to the positions of nucleotide	R33948, R52119, R52216, R53248,
.	residues shown in SEQ ID NO:527, and where b is	R53249, R71311, H04393, H04418,
	greater than or equal to a + 14.	H23196, H23309, H47118, R95161,
	greater than or equal to a * 1 th	H54791, H54843, H66487, H66488,
· ·		H87522, H87523, H92220, H97204,
1	·	H97637, H98041, N25008, N27036,
		N32850, N32940, N41677, N41803,
·		N52911, N55243, N55603, N59425,
1		N62367, N67146, N67527, N68040,
		N68109, N69439, N79136, W03264,
İ		W02511, W16533, W16511, W16949,
		W19590, W20032, W25683, W56022,
		W57870, W58141, W84752, W84757,
		W96458, W96558, N89892, N91494,
1.		AA035714, AA040577, AA040675,
1		AA043889, AA052991, AA053277,
	·	AA053702, AA062923, AA063530,
		AA074314, AA074909, AA074744,
		AA076274, AA098982, AA099025,
		AA146894, AA146893, AA160127,
		AA160126, AA160195, AA160196,
		AA169764, AA169385, AA179301,
		AA223348, AA233558, AA235471,
		1 ' '
		AA460676, AA420533, AA506563,
		AA523418, AA527621, AA528362,
		AA531060, AA532619, AA541282,
İ		AA552184, AA564466, AA564790,
		H98795, AA583450, AA613483,
		AA622733, AA627809, AA577550,
		AA578980, AA579413, AA714153,
L		AA721494, AA721786, AA737104,

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		AA738062, AA745852, AA746662,
		AA748113, AA814512, AA814515,
		AA848156, AA858182, AA877787,
		AA886219, AA886814. AA908510,
		AA919073, AA953828, AA971838,
ļ		AA974669, AA974937, AA975070,
		AA978156, AA985412, AA985429,
		AA989103, AA989168, AA975750,
l		AI053418, AI053736, AI053892,
		A1053967, A1053988, A1054073,
l	· ·	A1054111, F18748, A1096767.
		W16689, F17979, W26593, W74635,
	J	R29761, AA090571, AA090284.
İ	j	AA092279, AA092676, AA174176,
		AA206002, AA206857, AA206939,
		AA204847, AA204862, AA205665,
1		AA205777, C17805, AA215924.
		AA284942, AA285094, AA292514,
		AA293872, AA398296, AA401676,
		AA412021, AA450108. AA450173,
ŀ		AA477960, AA478675, AA479216,
		AA482218, AA608548, AA634838,
1		AA634910, AA634951, AA644321,
		AA664196, AA665979, AA668238,
j		AA668579, AA669764, AA669856,
	· ·	AA676279, AA630300, Z20366,
1		AA716371, AA716380, Z19906,
l		AA777040, AA778451, AA781061,
		AA845834, T25435, Z21568,
1	· ·	AA772588, AA917780, A1003327,
		AI016140, AI024969, AI032559,
		A1056850, A1088269, A1090536,
1	1	A1092597, A1093387, T15364, D29035,
		T27400, T27473, F02321, F06069,
		1
041162		T69476, AA773898, AA694154
841163	Preferably excluded from the present invention are	[70512, W58177, W58266, AA027003,
	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	AA047260, AA057146, AA076110, AA150122, AA150030, AA424246,
	, ,	AA425670, AA523788, AA554661,
	where a is any integer between 1 to 802 of SEQ ID	
İ	NO:528, b is an integer of 15 to 816, where both a and b correspond to the positions of nucleotide	AA582491, AA587000, AA633476, AA578397, AA662364, AA687611,
1	· · · · · · · · · · · · · · · · · · ·	AA729856, AA741041, AA806947,
j	residues shown in SEQ ID NO:528, and where b is	AA894899, AA922687, AA934486,
Ī	greater than or equal to a + 14.	
		AA946779, AA954606, AA962108,
1		AA988276, A1054171, AA436000,
1		AA436099, AA442324, AA451996,
1		AA722958, AA780203, T25797,
241162	D.C. III.	A1018410, A1024726, A1074321
841169	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
1	where a is any integer between 1 to 871 of SEQ ID	
1	NO:529, b is an integer of 15 to 885, where both a	i
		į
	and b correspond to the positions of nucleotide	
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:529, and where b is	
841172	and b correspond to the positions of nucleotide	T47968, H14181, H26893, N40884,

	· · · · · · · · · · · · · · · · · · ·	
	one or more polynucleotides comprising a nucleotide	Z42735
	sequence described by the general formula of a-b.	
1	where a is any integer between 1 to 728 of SEQ ID	
	NO:530. b is an integer of 15 to 742, where both a	,
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:530, and where b is	1
	greater than or equal to a + 14.	
841174	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 511 of SEQ ID	
	NO:531, b is an integer of 15 to 525, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:531, and where b is	·
	greater than or equal to a + 14.	
841179	Preferably excluded from the present invention are	
041177	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1911 of SEQ ID	
	NO:532, b is an integer of 15 to 1925, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:532, and where b is	
041102	greater than or equal to a + 14.	
841183	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	[
	where a is any integer between 1 to 488 of SEQ ID	
	NO:533, b is an integer of 15 to 502, where both a	
}	and b correspond to the positions of nucleotide	,
	residues shown in SEQ ID NO:533, and where b is	
	greater than or equal to a + 14.	
841186	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1786 of SEQ ID	
	NO:534, b is an integer of 15 to 1800, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:534, and where b is	
	greater than or equal to a + 14.	<u></u>
841204	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	 .
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2483 of SEQ ID	
	NO:535, b is an integer of 15 to 2497, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:535, and where b is	
	greater than or equal to a + 14.	
841206	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
i	where a is any integer between 1 to 4076 of SEQ ID	·
	NO:536, b is an integer of 15 to 4090, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:536, and where b is	,
	greater than or equal to a + 14.	·
841207		AA215286
011201	one or more polynucleotides comprising a nucleotide	111413200
	pine or more polynacieotides comprising a nucleotide	L

	harmon day that had a life of the	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 572 of SEQ ID	
	NO:537, b is an integer of 15 to 586, where both a	
	and b correspond to the positions of nucleotide	·
	residues shown in SEQ ID NO:537, and where b is	
	greater than or equal to a + 14.	
841211	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	,
	sequence described by the general formula of a-b,	,
	where a is any integer between 1 to 1236 of SEQ ID	
	NO:538, b is an integer of 15 to 1250, where both a	1
	and b correspond to the positions of nucleotide	,
	residues shown in SEQ ID NO:538, and where b is	·
	greater than or equal to a + 14.	
841225	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1336 of SEQ ID	
	NO:539, b is an integer of 15 to 1350, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:539, and where b is	· ·
	greater than or equal to a + 14.	
841229	Preferably excluded from the present invention are	
041229	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2495 of SEQ ID	
	NO:540, b is an integer of 15 to 2509, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:540, and where b is	
841237	greater than or equal to a + 14. Preferably excluded from the present invention are	H39746, H38765, H53680, H84385,
841237		
		H84386, H95751, H96427, H96428, N22709, N24033, N27417, N27531,
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1729 of SEQ ID	N31183, N34699, N35427, N40348,
	NO:541, b is an integer of 15 to 1743, where both a	N46995, N47385, W47664, W52613,
i	and b correspond to the positions of nucleotide	W58021, AA020909, AA032219,
	residues shown in SEQ ID NO:541, and where b is	AA032277, AA036745, AA053732,
	greater than or equal to a + 14.	AA055872, AA057318, AA062713,
	İ	AA070398, AA134055, AA132315,
		AA132625, AA149601, AA149602,
		AA494458, AA516430, AA534386,
	1	AA582804, AA581987, AA588838,
		AA631158, AA635970, AA577392,
		AA577494, AA857008, AA894813,
		AA933084, A1000994, N47386,
		D11495, D11593, D12071, D11877,
		D11882, D11902, AA456436,
		AA683214, AA890528, AA983938,
		A1074406, A1084728
841241	Preferably excluded from the present invention are	Γ64820, R18486, R48571, R48670,
	one or more polynucleotides comprising a nucleotide	R51358, R51464, R70428, R71854,
	sequence described by the general formula of a-b,	R77389, R77390, H18251, H18293,
	where a is any integer between 1 to 2196 of SEQ ID	H18401, H18402, H19764, H19765,
	NO:542, b is an integer of 15 to 2210, where both a	H21210, H21526, H24560, H25150,
	and b correspond to the positions of nucleotide	H26985, H28104, H30240, H30297,
		H30868, H30871, H40890, H41878,
	residues shown in SEQ ID NO:542, and where b is greater than or equal to a + 14.	H41879, H43721, H43811, H43814,

R84543, R85932, R87323, R93828, H49042, H49101, H51175, H51188, H468511, H75818, H80551, R80507, N41005, N45017, N56601, N70611, N70611, N74891, N93043, N93044, N94350, N98497, W04932, W21511, W21512, W24020, W31043, W47411, W47610, W47659, W47660, W48851, W48618, W52281, W56619, W63434, W68375, W70156, W70159, W84467, W84552, W90400, W94826, W906342, W906343, N91167, A016293, A017674, A025151, A025152, A027955, A031855, A031854, A035782, A037852, A037853, A031855, A031854, A035782, A037853, A031855, A031854, A035782, A038539, A04089669, A046918, A069509, A101608, A011873, A011837, A0			
H68511, H75818, H80551, N85061, N70611, N41005, N45017, N5601, N70611, N74891, N93043, N93044, N94350, N94897, W04932, W21511, W21512, W24020, W31043, W47411, W47610, W47669, W47660, W48851, W48618, W52281, W56619, W6331, W48618, W52281, W56619, W6331, W48618, W52281, W56619, W6331, W68375, W70156, W70195, W84467, W84552, W90400, W94826, W96342, W96343, N91167, AA016293, AA017674, AA025151, AA025152, AA027955, AA031855, AA031854, AA035782, AA027955, AA031855, AA031854, AA035782, AA031855, AA031854, AA035782, AA027955, AA031855, AA031854, AA035782, AA031855, AA031854, AA035782, AA059269, AA069418, AA069509, AA11608, AA114873, AA115697, AA13516, AA022968, AA458330, AA469966, AA463396, AA499116, AA03669, AA903116, AA003220, AA918099, AA928492, AA971856, AA973427, AA994099, A1016016, A1057267, AA069497, AA206877, AA368669, AA90316, AA003220, AA918099, AA928492, AA971856, AA973427, AA994099, A1016016, A1057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA946283, AA609652, AA708123, AA75465, AA522605, AA868271, AA884190, T03362, A1042345, A1042606, A106399, A1085641, A1089667, A1091380, A1091725, A1092820, A1092945, T23722, F103416, F04814, F07127, F08608, F12341 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3700 f SDC 1D NO-543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO-543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3700 f SDC 1D N0-543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO-544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the			R84543, R85932, R87323, R93828,
H68511, H75818, H80551, N85061, N70611, N41005, N45017, N5601, N70611, N74891, N93043, N93044, N94350, N94897, W04932, W21511, W21512, W24020, W31043, W47411, W47610, W47669, W47660, W48851, W48618, W52281, W56619, W6331, W48618, W52281, W56619, W6331, W48618, W52281, W56619, W6331, W68375, W70156, W70195, W84467, W84552, W90400, W94826, W96342, W96343, N91167, AA016293, AA017674, AA025151, AA025152, AA027955, AA031855, AA031854, AA035782, AA027955, AA031855, AA031854, AA035782, AA031855, AA031854, AA035782, AA027955, AA031855, AA031854, AA035782, AA031855, AA031854, AA035782, AA059269, AA069418, AA069509, AA11608, AA114873, AA115697, AA13516, AA022968, AA458330, AA469966, AA463396, AA499116, AA03669, AA903116, AA003220, AA918099, AA928492, AA971856, AA973427, AA994099, A1016016, A1057267, AA069497, AA206877, AA368669, AA90316, AA003220, AA918099, AA928492, AA971856, AA973427, AA994099, A1016016, A1057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA946283, AA609652, AA708123, AA75465, AA522605, AA868271, AA884190, T03362, A1042345, A1042606, A106399, A1085641, A1089667, A1091380, A1091725, A1092820, A1092945, T23722, F103416, F04814, F07127, F08608, F12341 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3700 f SDC 1D NO-543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO-543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3700 f SDC 1D N0-543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO-544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the	ŀ		H49042, H49101, H51175, H51188.
N41005, N45017, N56601, N70611, N74891, N93043, N93044, N94350, N98497, W04932, W21511, W21512, W24020, W31043, W31044, N94350, N98497, W04932, W21511, W21512, W24020, W31043, W47411, W47607, W47659, W47660, W68851, W48618, W52281, W56619, W56649, W68334, W68375, W70159, SW48616, W68452, W90400, W94826, W96342, W96343, N91167, AA016293, AA017674, AA025151, AA051515, AA031395, AA031856, AA056359, AA069269, AA069418, AA069418, AA069509, AA101608, AA114873, AA114837, AA114837, AA114857, AA114837, AA1145697, AA133516, AA220968, AA419091, A428836, AA507951, AA582836, AA640114, AA659114, AA836669, AA93136, AA903120, AA918099, AA101614, AA659114, AA836669, AA93136, AA903120, AA918099, AA101616, AA075267, AA069497, AA206877, AA218868, AA284782, AA971856, AA973427, AA994099, AU16016, AA057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA7768123, AA757619, AA757695, AA774425, AA776613, AA757695, AA774425, AA776613, AA775664, AA852435, AA852436, AA85243			
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AA11608, AA114873, AA114837, AA114837, AA114837, AA114837, AA114837, AA114837, AA114837, AA114837, AA114837, AA114837, AA1148530, AA460966, AA403966, AA463966, AA43956, AA419091, AA428836, AA507951, AA582836, AA640114, AA639114, AA83669, AA903182, AA903220, AA918099, AA928492, AA971856, AA973427, AA994099, AI016016, AI057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA75465, AA852435, AA852436, AA852604, AA852605, AA868271, AA884190, T03362, AI042345, AI042606, AI066399, AI086541, AI086697, AI091380, AI091727, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NC:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NC:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NC:543, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NC:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NC:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NC:544, and where b is greater than or equal to a + 14. 841260 ANA60554, AA605554, AA605555, AA492261, AA596073, AA600514, AA605554, AA605554, AA605555, AA492261, AA596073, AA600514, AA676927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			1 ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' '
AA115697, AA133516, AA20968, AA463596, AA463596, AA4619091, AA428836, AA607951, AA582836, AA640114, AA659114, AA836669, AA903136, AA903220, AA918099, AA92822, AA971829, AA971829, AA971836, AA973427, AA994099, A1016016, A1057267, AA069497, AA208877, AA218868, AA287438, AA28712, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757695, AA774425, AA774630, AA775465, AA852435, AA852436, AA852604, AA852605, AA868271, AA884190, T03362, A10422345, A10422345, A10422606, A1066399, A1082540, A1092820, A1092820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID N0:543, is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID N0:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID N0:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID N0:543, and where b is greater than or equal to a + 14. 841261 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID N0:543, and where b is greater than or equal to a + 14. 841261 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID N0:544, and where b is greater than or equal to a + 14. 841261 AA618211, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1		
A4438530, AA460966, AA463996, AA413991, AA28836, AA507951, AA582836, AA640114, AA659114, AA836669, AA903136, AA903220, AA918099, AA928492, AA971856, AA973427, AA994099, A1016016, A1057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774636, AA852435, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852436, AA852406, A1066399, A1086541, A1086967, A1091380, A1091725, A10923820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide scquence described by the general formula of a -b, where a is any integer between 1 to 1701 of 5EQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841261 AA80303, AA6035054, AA605555, AA92261, AA509073	l	·	
AA419091, AA428836, AA507951, AA582836, AA640114, AA659114, AA836669, AA903136, AA903220, AA918099, AA928492, AA971856, AA973427, AA994099, Al016016, Al057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA696522, AA708123, AA757619, AA757695, AA774425, AA774630, AA757695, AA774425, AA774630, AA757695, AA852435, AA852436, AA852604, AA852605, AA868271, AA884190, T03362, Al0942345, Al042606, Al066399, Al086541, Al086967, Al091380, Al091725, Al092820, Al092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 7175, where both a and b correspond to the positions of nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 RA1803373, AA460833776, AA872768, AA604012, AA612811, AA617927, AA618804, AA767954, AA769298, AA8404811, AA814647, AA833776, AA872768,	1		
AA582836, AA640114, AA659114, AA639114, AA836669, AA903136, AA903120, AA918099, AA928492, AA971856, AA973427, AA094099, Al016016, Al057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA775465, AA852405, AA852405, AA852406, AA852605, AA862271, AA884190, T03362, Al042345, Al042606, Al066399, Al086541, Al0866967, Al091380, Al091725, Al092820, Al092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Alo6399, Alo84081, Alo64081, Alo63996, Alo6955, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo63996, Alo64081, Alo			
AA836669, AA903136, AA903220, AA918099, AA928492, AA971856, AA973427, AA994099, A1016016, A1057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293424, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA775465, AA852435, AA852436, AA852604, AA852605, AA68271, AA884190, T03362, A1042345, A1042606, A1066399, A1086541, A1086967, A1091380, A1091725, A1092820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841261 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841261 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841261 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841262 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841261 Preferably excluded	1.		1 ' 1
A918099, AA928492, AA971856, AA973427, AA909999, A1016016, A1057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA6096522, AA708123, AA776630, AA775695, AA774425, AA776630, AA775695, AA774425, AA776630, AA775695, AA774425, AA776630, AA775695, AA774425, AA776630, AA775695, AA774425, AA776630, AA775695, AA774425, AA776630, AA775695, AA852435, AA852436, AA852604, AA852605, AA86271, AA884190, T03362, A1042345, A1042606, A1066399, A1086541, A1086967, A1091380, A1091725, A1092820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 ANS8962, ANS8961, AA19239, AA180323, AA460554, AA605955, AA492261, AA596073, AA604012, AA612811, AA6149277, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1		
AA973427, AA994099, Al016016, Al057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA77565, AA852436, AA852436, AA852404, AA852605, AA868271, AA884190, T03362, Al042345, Al042606, Al066399, Al086541, Al086697, Al091380, Al091725, Al092820, Al092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 AA058961, AA199299, AA804012, AA605541, AA605551, AA969298, AA804012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	`		AA836669, AA903136, AA903220,
A1057267, AA069497, AA206877, AA218868, AA284783, AA284712, AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA75465, AA852435, AA852436, AA852404, AA852605, AA868271, AA884190, T03362, A1042345, A1042606, A1066399, A1086541, A1086967, A1091380, A1091725, A1092820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:543, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A61261 A61274, A63947, A630697, AA606551, AA460555, AA492261, AA596073, AA601012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			AA918099, AA928492, AA971856,
AA218868, AA284783, AA284712, AA293434, AA2934042, AA402851, AA4454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA775465, AA852435, AA852436, AA852436, AA852436, AA852435, AA852436, AA852436, AA852435, AA852436, AA884190, T03362, A1042345, A1042606, A1066399, A1086541, A1086967, A1091380, A1091725, A1092820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 AA218868, AA284782, AA769281, AA882607, AA872768, AA869271, AA769284, AA769284, AA769284, AA769284, AA769298, AA884811, AA814647, AA833776, AA872768,			AA973427, AA994099, AI016016,
AA218868, AA284783, AA284712, AA293434, AA2934042, AA402851, AA4454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA775465, AA852435, AA852436, AA852436, AA852436, AA852435, AA852436, AA852436, AA852435, AA852436, AA884190, T03362, A1042345, A1042606, A1066399, A1086541, A1086967, A1091380, A1091725, A1092820, A1092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 AA218868, AA284782, AA769281, AA882607, AA872768, AA869271, AA769284, AA769284, AA769284, AA769284, AA769298, AA884811, AA814647, AA833776, AA872768,			AI057267, AA069497, AA206877,
AA293434, AA293042, AA402851, AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA77630, AA775465, AA852435, AA852436, AA852604, AA852605, AA868271, AA884190, T03362, AI042345, AI042606, AI066399, Al086541, AI086967, AI091380, AI091725, AI092820, AI092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide residues shown in SEQ ID NO:544, and where b is and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AN0:543, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AN0:543, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AN0:543, AN		<u>.</u>	· ·
AA454608, AA496283, AA609652, AA708123, AA757619, AA757695, AA774425, AA774630, AA775465, AA852435, AA852436, AA852604, AA852405, AA868271, AA884190, T03362, Al042345, Al042606, Al066399, Al086541, Al086967, Al091380, Al091725, Al092820, Al092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A058962, AA058961, AA149239, AA617812, AA0555614, AA617927, AA613804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1		
AA708123, AA757619, AA757695, AA774425, AA774630, AA775465, AA852435, AA852436, AA852604, AA852605, AA868271, AA884190, T03362, AI042345, AI042606, AI066399, AI086541, AI086967, AI091380, AI091725, AI092820, AI092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A058962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA617811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			1
AA774425, AA774630, AA775465, AA852435, AA852436, AA852604, AA852605, AA852606, AA852606, AI066399, AI086541, AI086967, AI091380, AI091725, AI092820, AI092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AN58962, AA058961, AA149239, AA1603554, AA460555, AA492261, AA596073, AA604012, greater than or equal to a + 14. AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			1 1
AA852435, AA852436, AA852604, AA852605, AA868271, AA884190, T03362, AI042345, AI042606, AI066399, AI086541, AI086967, AI091380, AI091725, AI092820, AI092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. ANS862435, AA852436, AA868271, AA884190, T03362, IN091380, AI091725, AI092820, AI091282, F04814, F07127, F08608, F12341 F07127, F08608, F12341 F193673, R01175, R01287, R72262, R72263, H53584, H53905, N57686, N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			
AA852605, AA868271, AA884190, T03362, Al042345, Al042606, Al066399, Al086541, Al086967, Al091380, Al091725, Al092820, Al092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 ANS8962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			1
T03362, AI042345, AI042606, AI066399, AI086541, AI086967, AI091380, AI091725, AI092820, AI092945, T23722, F03416, F04814, F07127, F08608, F12341 841259 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A058962, AA058961, AA19239, AA180233, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			
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A1092945, T23722, F03416, F04814, F07127, F08608, F12341 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A1092945, T23722, F03416, F04814, F07127, F08608, F12341 T93673, R01175, R01287, R72262, R72263, H53584, H53905, N57686, N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A058962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1		
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. ANOSS962, AA058961, AA149239, AA160555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	l		A1092945, T23722, F03416, F04814,
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Area of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Area of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14.			F07127, F08608, F12341
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Area of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Area of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14.	841259	Preferably excluded from the present invention are	
sequence described by the general formula of a-b, where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Article 175, R01287, R72262, R72263, H53584, H53905, N57686, N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA160554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			
where a is any integer between 1 to 1701 of SEQ ID NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A058962, A058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			
NO:543, b is an integer of 15 to 1715, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A0058962, A0058961, AA149239, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. A4058962, A4058961, AA149239, AA460555, A4492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			·
residues shown in SEQ ID NO:543, and where b is greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,			'
greater than or equal to a + 14. 841260 Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are 193673, R01175, R01287, R72262, R72263, H53584, H53905, N57686, N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	İ		
Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. Preferably excluded from the present invention are	ł		
one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. R72263, H53584, H53905, N57686, N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	L		
sequence described by the general formula of a-b, where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. N59657, N63715, N98804, W86302, W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	841260		
where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1		
where a is any integer between 1 to 3095 of SEQ ID NO:544, b is an integer of 15 to 3109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. W86653, W87312, AA055614, AA058962, AA058961, AA149239, AA180323, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1	sequence described by the general formula of a-b,	N59657, N63715, N98804, W86302,
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	l		W86653, W87312, AA055614,
and b correspond to the positions of nucleotide residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AA180323, AA460554, AA460555, AA492261, AA596073, AA604012, AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	l		AA058962, AA058961, AA149239.
residues shown in SEQ ID NO:544, and where b is greater than or equal to a + 14. AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	l		
greater than or equal to a + 14. AA612811, AA617927, AA631804, AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	1		
AA767954, AA769298, AA804811, AA814647, AA833776, AA872768,	l		AA612811, AA617927, AA631804
AA814647, AA833776, AA872768,	1	beard, man or adon to a . 14.	AA767954 AA769208 AA804811
AA873458, AA876551, AA886069,			AA814647 AA833776 AA833720
AA880009,	· .		A 873458 A 876561 A 4006060
	L		PERO13430, AM010331, AM880009,

		
841264	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1162 of SEQ ID	AA932445. AA976417, AA989268, A1055853. D80933. A1088938. A1096484. AA215901, AA393250, AA435612, AA449044, AA449758. AA653318. AA678103, AA678744, AA705036, AA854081, AA789188. AA813062. AA868902, A1023192. A1033456. A1090508. Z28555, T25877, D30980, D31048. D31377, F00724, AA682530. AA694353
	NO:545, b is an integer of 15 to 11-76, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:545, and where b is greater than or equal to a + 14.	
841275	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1721 of SEQ ID NO:546, b is an integer of 15 to 1735, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:546, and where b is greater than or equal to a + 14.	
841311	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1034 of SEQ ID NO:547, b is an integer of 15 to 1048, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:547, and where b is greater than or equal to a + 14.	
841313	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 722 of SEQ ID NO:548, b is an integer of 15 to 736, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:548, and where b is greater than or equal to a + 14.	
841317	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2217 of SEQ ID NO:549, b is an integer of 15 to 2231, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:549, and where b is greater than or equal to a + 14.	T78127, R31279, R31890, R38014, R68187, R68186, R68960, R81444, R81647, H03085, H42975, N22228, N35405, N40226, N52138, N66461, N66470, W48764, W49783, W58388, AA044222, AA044341, AA131687, AA131731, AA224224, AA224527, AA469092, AA580878, AA573581, AA863153, AA903745, AA971415, C03879, AA249392, AA448556, AA449703, F22605, AA723322, AA904943, Z18868, AA971554, AA991799, A1015846, A1037913, A1056007, A1082497, A1090170, A1095394

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841322	Preferably excluded from the present invention are	R21970, R83459, H65911, W76286,
	one or more polynucleotides comprising a nucleotide	AA182592. AA281797. AA281874,
	sequence described by the general formula of a-b,	AA291943. H65824, AA580660.
	where a is any integer between 1 to 1802 of SEQ ID	AA748474, AA829390, AA293389,
	NO:550, b is an integer of 15 to 1816, where both a	AA401755, AA910004, AA994494,
	and b correspond to the positions of nucleotide	AI005165, AI081877
f	residucs shown in SEQ ID NO:550, and where b is	
1	greater than or equal to a + 14.	
841331	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
İ	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2596 of SEQ ID	
	NO:551, b is an integer of 15 to 2610, where both a	
1	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:551, and where b is	
	greater than or equal to a + 14.	
841332	Preferably excluded from the present invention are	
041332	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	j
ŀ	where a is any integer between 1 to 4007 of SEQ ID	
	NO:552, b is an integer of 15 to 4021, where both a	
ł	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:552, and where b is	
841338	greater than or equal to a + 14.	
841338	Preferably excluded from the present invention are	
ļ	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1766 of SEQ ID	
ĺ	NO:553, b is an integer of 15 to 1780, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:553, and where b is	
	greater than or equal to a + 14.	
841345	Preferably excluded from the present invention are	1
l	one or more polynucleotides comprising a nucleotide	-
1	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3699 of SEQ ID	
	NO:554, b is an integer of 15 to 3713, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:554, and where b is	
	greater than or equal to a + 14.	
841349	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1983 of SEQ ID	
	NO:555, b is an integer of 15 to 1997, where both a	
·	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:555, and where b is	
	greater than or equal to a + 14.	
841355	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 892 of SEQ ID	
	NO:556, b is an integer of 15 to 906, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:556, and where b is	
	greater than or equal to a + 14.	
841417	Preferably excluded from the present invention are	
V (171/	p research excitated from the present invention are	

	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
l	where a is any integer between 1 to 3470 of SEQ ID	{
	NO:557, b is an integer of 15 to 3484, where both a	
ĺ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:557, and where b is	
	greater than or equal to a + 14.	
841548	Preferably excluded from the present invention are	AA223588
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
ĺ	where a is any integer between 1 to 776 of SEQ ID	
ĺ	NO:558, b is an integer of 15 to 790, where both a	·
	and b correspond to the positions of nucleotide	
ł	residues shown in SEQ ID NO:558, and where b is	
	greater than or equal to $a + 14$.	
841632	Preferably excluded from the present invention are	
641032	one or more polynucleotides comprising a nucleotide	
i	sequence described by the general formula of a-b,	•
	where a is any integer between 1 to 544 of SEQ ID	
	NO:559, b is an integer of 15 to 558, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:559, and where b is	
041663	greater than or equal to a + 14.	1115050 110070C NIZOCAC NIZAZOO
841662	Preferably excluded from the present invention are	H15850, H99706, N78646, W74702,
	one or more polynucleotides comprising a nucleotide	W94916, AA809695
l	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 520 of SEQ ID	
	NO:560, b is an integer of 15 to 534, where both a	
I	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:560, and where b is	
	greater than or equal to a + 14.	
841771	Preferably excluded from the present invention are	T50029, T67900, T74699, T74819,
	one or more polynucleotides comprising a nucleotide	T88802, T81298, T84439, T95656,
		R06092, R06196, R14563, R14966,
		R 14970, R 16465, R 38948, R 40957,
	NO:561, b is an integer of 15 to 3043, where both a	R40957, R63975, R64085, R66362,
	and b correspond to the positions of nucleotide	R66363, R67505, H17644, H17758,
•	residues shown in SEQ ID NO:561, and where b is	R92097, H48240, H48331, H49625,
	greater than or equal to a + 14.	H49715, H61167, H62068, H69147,
		N25753, N36472, N69035, N71493,
		N92970, N98567, N99536, W00665,
		W24251, W40582, W45462, W45538,
		W45525, W45687, W44315, W57971,
		W57944, W70012, W70013, W86733,
	·	AA044684, AA071192, AA071199,
		AA190325, AA191520, AA533197,
,		AA558210, AA581106, AA581161,
•		AA577119, AA857551, AA878885,
		AA936839, AA975697, D78980,
		W28535, C02075, C17857
841827	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
		1
	where a is any integer between 1 to 1372 of SEO ID	
	where a is any integer between 1 to 1372 of SEQ ID INO:562, b is an integer of 15 to 1386, where both a	,
	where a is any integer between 1 to 1372 of SEQ ID NO:562, b is an integer of 15 to 1386, where both a and b correspond to the positions of nucleotide	,

	greater than or equal to a + 14.	
841835	Preferably excluded from the present invention are	
}	one or more polynucleotides comprising a nucleotide	<u> </u>
	sequence described by the general formula of a-b.	
İ	where a is any integer between 1 to 2624 of SEQ ID	
ļ	NO:563, b is an integer of 15 to 2638, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:563, and where b is	
	greater than or equal to a + 14.	
842259	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 677 of SEQ ID	
	NO:564, b is an integer of 15 to 691, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:564, and where b is	·
	greater than or equal to a + 14.	
842463	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
İ	where a is any integer between 1 to 1953 of SEQ ID	
	NO:565, b is an integer of 15 to 1967, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:565, and where b is	
	greater than or equal to a + 14.	
842595	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1320 of SEQ ID	
	NO:566, b is an integer of 15 to 1334, where both a	
	and b correspond to the positions of nucleotide	•
	residues shown in SEQ ID NO:566, and where b is	
0.40700	greater than or equal to a + 14.	
842722	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1596 of SEQ ID	
	NO:567, b is an integer of 15 to 1610, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:567, and where b is	
042016	greater than or equal to a + 14.	
842815	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1398 of SEQ ID	
	NO:568, b is an integer of 15 to 1412, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:568, and where b is	
842818	greater than or equal to a + 14.	
042010	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1111 of SEQ ID	•
	NO:569, b is an integer of 15 to 1125, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:569, and where b is	
	greater than or equal to a + 14.	

843251	Preferably excluded from the present invention are	
E	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1902 of SEQ ID	
	NO:570, b is an integer of 15 to 1916, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:570, and where b is	
	greater than or equal to a + 14.	
843422	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1239 of SEQ ID	
	NO:571, b is an integer of 15 to 1253, where both a	\
	and b correspond to the positions of nucleotide	
Ì	residues shown in SEQ ID NO:571, and where b is	
	greater than or equal to a + 14.	
843784	Preferably excluded from the present invention arc	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1999 of SEQ ID	
	NO:572, b is an integer of 15 to 2013, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:572, and where b is	
	greater than or equal to a + 14.	
844017	Preferably excluded from the present invention are	AA075932
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 655 of SEQ ID	
	NO:573, b is an integer of 15 to 669, where both a	
	and b correspond to the positions of nucleotide	}
	residues shown in SEQ ID NO:573, and where b is	
	greater than or equal to a + 14.	
844138	Preferably excluded from the present invention are	T54096, T54187, T54360, T39143,
	one or more polynucleotides comprising a nucleotide	T40432, T90493, T90589, T89428,
	sequence described by the general formula of a-b,	T89794, T80000, R00221, R00327,
	where a is any integer between 1 to 2418 of SEQ ID	R25952, R26450, R26761, R28459,
	NO:574, b is an integer of 15 to 2432, where both a	R55293, R55390, R73233, H42630,
	and b correspond to the positions of nucleotide	H44454, H44498, R83525, R86282,
	residues shown in SEQ ID NO:574, and where b is	H85785, N33586, N34419, N36244,
	greater than or equal to a + 14.	N48653, N49430, W51915, AA055530,
		AA055939, AA069732, AA100817,
		AA122084, AA121407, AA126332,
		AA133329, AA134151, AA134152,
		AA134714, AA136470, AA136960,
		AA157850, AA157906, AA157976,
		AA159365, AA171854, AA187219,
		AA186342, AA250818, AA464565,
		AA464666, AA428826, AA429361,
		AA491863, AA505512, AA524490,
		AA558038, AA581979, AA588712,
		AA593885, AA601110, AA573930,
		AA577156, AA578735, AA689519,
		AA730155, AA768486, AA805061,
		AA826981, AA865985, AA931167,
		AA947324, AA953202, AA961105,
		AA962413, AA976440, AA977760,
		AI032134, AI053416, AI053575,

		A 1054013 A 1054146 A 1054201
		A1054013, A1054146, A1054281,
		U46376, W22126, C00371, C05283,
}		AA641416, AA643346, AA292261,
1		AA421818, AA496452. AA496521.
İ		AA653437, AA664399, AA680123.
1		AA431832, AA434143, AA678582,
1		AA705952, AA679763, AA733019,
		AA781645, AA813232, AA833597.
	· ·	AA844624, AI024151, AI038232,
		A1042551, A1080152, A1086490.
		T24101, F03522, F07244
844166	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
,	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1358 of SEQ ID	
	NO:575, b is an integer of 15 to 1372, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:575, and where b is	·
L	greater than or equal to a + 14.	
844194	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2006 of SEQ ID	
1	NO:576, b is an integer of 15 to 2020, where both a	
	and b correspond to the positions of nucleotide	
<u> </u>	residues shown in SEQ ID NO:576, and where b is	
	greater than or equal to a + 14.	
844394	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	1
1	sequence described by the general formula of a-b,	-
	where a is any integer between 1 to 3147 of SEQ ID	
1	NO:577, b is an integer of 15 to 3161, where both a	
	and b correspond to the positions of nucleotide	
1	residues shown in SEQ ID NO:577, and where b is	
	greater than or equal to a + 14.	
844450	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
•	sequence described by the general formula of a-b,	`
1	where a is any integer between 1 to 2032 of SEQ ID	
	NO:578, b is an integer of 15 to 2046, where both a	
İ	and b correspond to the positions of nucleotide	
Į.	residues shown in SEQ ID NO:578, and where b is	
	greater than or equal to a + 14.	
844534	Preferably excluded from the present invention are	
דננדי ע	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,]
	where a is any integer between 1 to 288 of SEQ ID	
	NO:579, b is an integer of 15 to 302, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:579, and where b is	1
044525	greater than or equal to a + 14. Preferably excluded from the present invention are	
844535	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 3053 of SEQ ID	
	NO:580, b is an integer of 15 to 3067, where both a	
L	and b correspond to the positions of nucleotide	l

	residues shown in SEQ ID NO:580, and where b is	
	greater than or equal to a + 14.	
844644	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b.	
ĺ	where a is any integer between 1 to 1560 of SEQ ID	
	NO:581, b is an integer of 15 to 1574, where both a	
Ì	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:581, and where b is	
	greater than or equal to a + 14.	
844653	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	·
	sequence described by the general formula of a-b,	}
ļ	where a is any integer between 1 to 946 of SEQ ID	
	NO:582, b is an integer of 15 to 960, where both a	
İ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:582, and where b is	
	greater than or equal to a + 14.	
844659	Preferably excluded from the present invention are	
1	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 527 of SEQ ID	
	NO:583, b is an integer of 15 to 541, where both a	
	and b correspond to the positions of nucleotide	,
	residues shown in SEQ ID NO:583, and where b is	
	greater than or equal to a + 14.	
844796	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2954 of SEQ ID	
	NO:584, b is an integer of 15 to 2968, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:584, and where b is	
ł	greater than or equal to a + 14.	
844812	Preferably excluded from the present invention are	
p	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2594 of SEQ ID	•
	NO:585, b is an integer of 15 to 2608, where both a	
•	and b correspond to the positions of nucleotide	·
	residues shown in SEQ ID NO:585, and where b is	
	greater than or equal to a + 14.	
944904		
844894	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	•
	sequence described by the general formula of a-b,	
•	where a is any integer between 1 to 1879 of SEQ ID	
	NO:586, b is an integer of 15 to 1893, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:586, and where b is	
045361	greater than or equal to a + 14.	T02072 T02161 T6276 T7276
845361	Preferably excluded from the present invention are	[F93072, T93161, T69748, T70732,
	one or more polynucleotides comprising a nucleotide	R01200, R01312, R05457, R05477,
	sequence described by the general formula of a-b,	R05584, R43190, R43190, R65942,
	where a is any integer between 1 to 2449 of SEQ ID	R75719, R78234, H03875, H03876,
	NO:587, b is an integer of 15 to 2463, where both a	H15845, H16155, H17787, H40269,
	and b correspond to the positions of nucleotide	H45881, R84787, R92493, R92931,
	residues shown in SEQ ID NO:587, and where b is	H58301, H58912, H58913, H62257,

H67051, H68135, H81385, H83681. greater than or equal to a + 14. H91363. H96711, N20348, N22509. N27952. N28616, N31997, N32005, N36007, N39356, N40718, N70011, N70094. N92576, N99870, W00896, W00925, W04623, W25220, W31522, W37278, W37791, W38868, W52654, W51751, AA017158, AA019458, AA022914, AA022915, AA037370, AA037502, AA045696, AA045697. AA046013, AA054565, AA054625, AA069778, AA079736, AA081087, AA081144, AA100055, AA100504, AA100334, AA115581, AA115554, AA126149. AA126373, AA133101, AA130558, AA136439, AA151673, AA151821, AA151822, AA159031, AA165200, AA165201, AA176477, AA176498, AA176771, AA176830, AA182601, AA176736, AA187943, AA188578, AA188675, AA190342, AA190343, AA195091, AA213662, AA213715, AA232222, AA426516, AA424760, AA483564, AA490859, AA491042, AA505249, AA507988, AA508858, AA513433, AA514771, AA514785, AA514980, AA527545, AA534100, AA554008, AA557148, AA584946, AA586481, AA587849, AA588781, AA593916, AA605049, AA604893, AA617650, AA568567, AA621979, AA627588, AA578585, AA578744, AA661910, AA729355, AA729902, AA736994, AA738388, AA740375, AA741213, AA760943, AA830401, AA834201, AA834208, AA834250, AA864864, AA888527, AA906940, AA922073, AA927272, AA931625, AA933055, AA932772, AA936861, AA938504, AA975187, AA977857, AA975594, AI000724, AI014600, AI017381, AI066441, D82733, U47688, N83708, N83790, N85010, W22533, W23255, N86314, N87393, N88971, AA642249, AA642903, AA090403, AA091011, AA095990, AA205824, AA204931, AA643262, AA648446, AA216706, AA219615, AA249170, C75338, AA599187, AA668746, AA670340, AA405611, AA405150, AA708635, AA716044, AA722076, AA722829, AA725716, AA**7**81064, AA844379, A1037987, A1039577, A1078722, A1077655, A1080306, A1084320, A1085219, A1093296, A1093479, A1095168, A1095267, D29018, F02782

		F06502. F00762, F00966
845620	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1931 of SEQ ID	•
	NO:588, b is an integer of 15 to 1945, where both a	
	and b correspond to the positions of nucleotide	1
	residues shown in SEQ ID NO:588, and where b is	
	greater than or equal to a + 14.	
845639	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 802 of SEQ ID	
	NO:589, b is an integer of 15 to 816, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:589, and where b is	
	greater than or equal to a + 14.	
845660	Preferably excluded from the present invention are	
0.5000	one or more polynucleotides comprising a nucleotide	·
•	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2293 of SEQ ID	
	NO:590. b is an integer of 15 to 2307, where both a	
	and b correspond to the positions of nucleotide	ļ
	residues shown in SEQ ID NO:590, and where b is	
	greater than or equal to a + 14.	
845720		
043720	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1424 of SEQ ID	
	NO:591, b is an integer of 15 to 1438, where both a	•
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:591, and where b is	
245505	greater than or equal to a + 14.	
845785	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1064 of SEQ ID	
	NO:592, b is an integer of 15 to 1078, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:592, and where b is	
	greater than or equal to a + 14.	
845897	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	·
	where a is any integer between 1 to 2478 of SEQ ID	
	NO:593, b is an integer of 15 to 2492, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:593, and where b is	_
	greater than or equal to a + 14.	
345922	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1890 of SEQ ID	
	NO:594, b is an integer of 15 to 1904, where both a	
	and b correspond to the bositions of nucleotide	
	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:594, and where b is	

846016	Preferably excluded from the present invention are	
	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 323 of SEQ ID	
	NO:595, b is an integer of 15 to 337, where both a	
ļ	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:595, and where b is	
	greater than or equal to a + 14.	
846040	Preferably excluded from the present invention are	
l	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 1274 of SEQ ID	
	NO:596, b is an integer of 15 to 1288, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:596, and where b is	
	greater than or equal to a + 14.	
846073	Preferably excluded from the present invention are	T83567, T83771, R51147, N26938,
	one or more polynucleotides comprising a nucleotide	N32715, N36666. W57781, W74108,
1	sequence described by the general formula of a-b,	AA082091, AA425613
	where a is any integer between 1 to 1038 of SEQ ID	,
	NO:597, b is an integer of 15 to 1052, where both a	
	and b correspond to the positions of nucleotide	•
	residues shown in SEQ ID NO:597, and where b is	
	greater than or equal to a + 14.	
846257	Preferably excluded from the present invention are	
· ·	one or more polynucleotides comprising a nucleotide	
	sequence described by the general formula of a-b,	
	where a is any integer between 1 to 2079 of SEQ ID	
	NO:598, b is an integer of 15 to 2093, where both a	
	and b correspond to the positions of nucleotide	
	residues shown in SEQ ID NO:598, and where b is	
	greater than or equal to a + 14.	

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Polynucleotide and Polypeptide Variants

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The present invention is directed to variants of the polynucleotide sequence disclosed in SEQ ID NO:X or the complementary strand thereto, and/or the cDNA sequence contained in a cDNA clone contained in the deposit.

The present invention also encompasses variants of the cancer polypeptide sequence disclosed in SEQ ID NO:Y, a polypeptide sequence encoded by the polynucleotide sequence in SEQ ID NO:X, and/or a polypeptide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, the nucleotide coding sequence in SEO ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the related cDNA contained in a deposited library or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEO ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA in the related cDNA contained in a deposited library, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polypeptides encoded by these nucleic acid molecules are also encompassed by the invention. In another embodiment, the invention encompasses nucleic acid molecules which comprise or alternatively consist of, a polynucleotide which hybridizes under stringent hybridization conditions, or alternatively, under low stringency conditions, to the nucleotide coding sequence in SEO ID NO:X, the nucleotide coding sequence of the related cDNA clone contained in a deposited library, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEO ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA in the related cDNA clone contained in a deposited library, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which

hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

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The present invention is also directed to polypeptides which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to, for example, the polypeptide sequence shown in SEQ ID NO:Y, a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the cDNA in the related cDNA clone contained in a deposited library, and/or polypeptide fragments of any of these polypeptides (e.g., those fragments described herein). Polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these polypeptides under stringent hybridization conditions, or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be, for example, an entire sequence referred to in Table 1, an ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be

compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other

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manual corrections are to made for the purposes of the present invention.

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By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence in SEO ID NO:Y or a fragment thereof, the amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237- 245(1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences

truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C- terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which less than 50, less

than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as E. coli).

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Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, as discussed herein, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptide of the present invention without substantial loss of biological function. The authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, as discussed herein, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more

biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

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Thus, the invention further includes polypeptide variants which show a functional activity (e.g., biological activity) of the polypeptide of the invention of which they are a variant. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity.

The present application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein or fragments thereof, (e.g., including but not limited to fragments encoding a polypeptide having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having functional activity include, inter alia, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) in situ hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); and (3) Northern Blot analysis for detecting mRNA expression in specific tissues.

Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, which do, in fact, encode a polypeptide having a functional activity of a polypeptide of the invention.

Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA in the related cDNA clone contained in a

deposited library, the nucleic acid sequence referred to in Table 1 (SEQ ID NO:X), or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

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The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side

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chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr. Met, and Gly. Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

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For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

A further embodiment of the invention relates to a polypeptide which comprises the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions. Of course it is highly preferable for a polypeptide to have an amino acid sequence which comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, and/or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1

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amino acid substitutions. In specific embodiments, the number of additions, substitutions, and/or deletions in the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein), an amino acid sequence encoded by SEQ ID NO:X or fragments thereof, and/or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library or fragments thereof, is 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, conservative amino acid substitutions are preferable.

Polynucleotide and Polypeptide Fragments

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The present invention is also directed to polynucleotide fragments of the cancer polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers, for example, to a polynucleotide having a nucleic acid sequence which: is a portion of the cDNA contained in a depostied cDNA clone; or is a portion of a polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in a deposited cDNA clone; or is a portion of the polynucleotide sequence in SEQ ID NO:X or the complementary strand thereto; or is a polynucleotide sequence encoding a portion of the polyneptide of SEO ID NO:Y; or is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto. The nucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, at least about 100 nt, at least about 125 nt or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from, for example, the sequence contained in the cDNA in a related cDNA clone contained in a deposited library, the nucleotide sequence shown in SEO ID NO:X or the complementary stand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 150, 175, 200, 250, 500, 600, 1000, or 2000 nucleotides in length) are also encompassed by the invention.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700,701-750, 751-800, 800-850, 851-900,

901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, and 3551 to the end of SEQ ID NO:X, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity) of the polypeptide encoded by the polynucleotide of which the sequence is a portion. More preferably, these fragments can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides or fragments.

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Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700,701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, and 3551 to the end of the cDNA nucleotide sequence contained in the deposited cDNA clone, or the complementary strand thereto. In this context "about" includes the particularly recited range, or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity) of the polypeptide encoded by the cDNA

nucleotide sequence contained in the deposited cDNA clone. More preferably, these fragments can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these fragments under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides or fragments.

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In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y, a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, and/or encoded by the cDNA contained in the related cDNA clone contained in a deposited library. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, an amino acid sequence from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, and 1181 to the end of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either terminus or at both termini. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

Even if deletion of one or more amino acids from the N-terminus of a protein results in modification of loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained when less than the majority of the residues of the complete or mature polypeptide are

removed from the N-terminus. Whether a particular polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted N-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

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Accordingly, polypeptide fragments of the invention include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, and/or a polypeptide encoded by the cDNA contained in the related cDNA clone contained in a deposited library). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y), and m is defined as any integer ranging from 2 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification of loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example the ability of the shortened mutein to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic

activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

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Accordingly, the present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, and/or a polypeptide encoded by the cDNA contained in deposited cDNA clone referenced in Table 1). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and where n corresponds to the position of an amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID NO:Y), and/or the cDNA in the related cDNA clone contained in a deposited library, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Any polypeptide sequence contained in the polypeptide of SEQ ID NO:Y, encoded by the polynucleotide sequences set forth as SEQ ID NO:X, or encoded by the cDNA in the related cDNA clone contained in a deposited library may be analyzed to determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide encoded by a polynucleotide sequence of SEQ ID NO:X, or the cDNA in a deposited cDNA clone may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; http://www.dnastar.com/).

Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions, Chou-Fasman alpha-regions, beta-regions, and turn-regions, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Eisenberg alpha- and

beta-amphipathic regions, Karplus-Schulz flexible regions, Emini surface-forming regions and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.

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Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Preferred polypeptide fragments of the invention are fragments comprising, or alternatively consisting of, an amino acid sequence that displays a functional activity of the polypeptide sequence of which the amino acid sequence is a fragment.

By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of SEQ ID NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Table 4.

Sequence/	Epitope
Contig ID	
507291	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 843 as
	residues: Pro-12 to Pro-20, Lys-27 to Gly-34. Pro-67 to Arg-72, Asp-102 to Thr-111,
	Asp-136 to Gly-142, Ser-153 to Pro-158.
508000	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 844 as
·	residues: Ala-16 to Trp-35.
518325	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 845 as
	residues: Glu-60 to Asp-67.
523111	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 846 as
	residues: Scr-1 to Gln-10.
532211	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 848 as
	residues: Cys-17 to Arg-22.
532247	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 849 as
	residues: Val-4 to His-10.
537932	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 850 as
640117	residues: Ser-62 to Gly-68.
540117	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 851 as
547710	residues: Pro-24 to Arg-30, Met-101 to Phe-106, Thr-138 to Asn-153. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 852 as
347710	residues: Asp-1 to Arg-7, Glu-25 to His-31, Ile-51 to Lys-56, Pro-61 to Pro-67, Gly-
	113 to Thr-119, Lys-125 to Asp-130, His-375 to Gly-340, Arg-364 to Pro-371.
551747	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 853 as
331747	residues: Lys-79 to Ala-88, Ser-109 to Leu-125, Asp-155 to Lys-163, Tyr-211 to Thr-
	219. Pro-221 to Ala-226.
552799	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 854 as
	residues: Gln-81 to Thr-114. Gln-200 to Arg-206.
553243	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 855 as
	residues: Ala-43 to Asp-48, Asp-64 to Lys-69, His-88 to Thr-94, Ala-107 to Phe-113,
	Leu-117 to Ser-125, Thr-132 to Glu-138, Ser-169 to Trp-181, Ser-194 to Thr-200.
553368	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 856 as
	residues: Ser-52 to Arg-57, Leu-76 to Gly-82, Ser-91 to Glu-96, Tyr-132 to Ala-147.
554349	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 857 as
	residues: Ala-31 to Gly-36, Ala-68 to Tyr-75, Gln-121 to Asp-127.
558491	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 858 as
	residues: Pro-1 to Arg-10.
558983	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 859 as
500200	residues: Pro-37 to Gly-42, Val-67 to Lys-84, Gln-122 to Gly-127.
589390	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 862 as
	residues: Glu-14 to Asn-19, Arg-68 to Ser-74, Ser-79 to Ala-84, Lys-95 to Ile-101, Lys-125 to Glu-138.
596882	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 863 as
	residues: Lys-15 to Lys-23, Pro-29 to Gly-34.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 864 as
	residues: Lcu-1 to Pro-13, Thr-64 to Gly-70, Lys-119 to Arg-130.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 865 as
	residues: Ser-1 to Lys-6, Pro-16 to Ser-23, Arg-49 to Glu-58.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 867 as
	residues: Arg-1 to Gly-9, Glu-27 to Gly-36, Pro-72 to Phe-86, Pro-104 to Cys-111,
	Gln-145 to Lys-162, Arg-226 to Trp-233.
652156	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 871 as
	residues: Asn-30 to Ile-43, Ile-76 to Lys-81.
653010	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 872 as

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655004	residues: Ser-1 to Ala-10.
655904	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 873 as
	residues: Ala-21 to Cys-27, Ser-76 to Gly-87, Ser-112 to Trp-121, Trp-128 to Asn-
	133. Glu-225 to Cys-231, Tyr-238 to Cys-248, Lys-269 to Asp-279, Phe-292 to Thr-
657952	298, Cys-357 to Ala-362, Pro-383 to Pro-388, Lys-412 to Lys-420.
657852	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 874 as
666414	residues: Arg-10 to Lys-22, Gln-48 to Glu-53, Arg-73 to Asn-86.
000414	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 875 as residues: Asn-9 to Lys-19, Arg-27 to Gly-32, Ser-58 to Thr-70, Ala-81 to Pro-86.
670188	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 877 as
070100	residues: Asn-68 to Ser-75.
670279	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 878 as
0.0217	residues: Lys-86 to Lys-91, Glu-101 to Val-120, Ala-130 to Glu-136.
670729	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 879 as
	residues: Ala-116 to Asp-134.
676496	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 881 as
	residues: Ilc-I to Arg-8.
678248	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 883 as
	residues: Ala-16 to Lys-22, Tyr-30 to Asn-35, Asp-61 to Val-70, Arg-129 to Asn-135,
	Thr-142 to Gly-148.
683668	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 884 as
	residues: Ser-3 to Gly-28, Gly-46 to Pro-56, Gly-70 to Ile-92, Gln-102 to Ser-117, Ala-
	123 to Pro-129, Pro-135 to Leu-140, Pro-150 to Asp-158, Pro-165 to Pro-177, Gln-188
	to Asp-205, Ile-230 to Arg-245, His-251 to Trp-260, Asp-262 to Cys-267, Asn-296 to
	Arg-307, Glu-322 to Pro-330, Ile-351 to Asn-357, Asp-363 to Leu-369, Glu-386 to
	Phe-391, Lys-415 to Ser-420.
693172	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 885 as
	residues: Arg-11 to Arg-18, Pro-51 to Lys-58.
694303	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 886 as
	residues: Pro-12 to Ser-17, Leu-30 to Cys-39, Val-49 to Pro-54, Pro-67 to Leu-73, Pro-
605042	84 to Gln-90, His-99 to Leu-109.
695042	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 887 as
699799	residues: Scr-4 to Trp-28, Pro-51 to Leu-56, Asn-64 to His-70. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 888 as
077777	residues: Gln-17 to Phe-25, Glu-42 to Tyr-48, Val-52 to Gly-57, Pro-67 to Ser-73, Thr-
•	97 to Gln-106, Gln-113 to Leu-123, Arg-171 to Asp-178, Arg-184 to Leu-191, Ile-195
	to Phe-203, Lys-212 to Glu-217, Ala-236 to Asp-244, Arg-255 to Leu-260, Lys-266 to
	His-273, Glu-357 to Glu-363.
703015	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 890 as
•	residues: Pro-27 to Asp-37, Gly-55 to Pro-61, His-96 to Ala-101, Glu-151 to Asn-156,
	Tyr-166 to Cys-178.
706391	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 891 as
	residues: Pro-22 to Ala-34, Pro-40 to Glu-52.
706924	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 893 as
	residues: Gly-1 to Gly-9, Gln-21 to Met-27.
707642	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 894 as
	residues: Glu-33 to Lys-40, Asn-55 to Lys-64, Tyr-104 to Cys-110, Ser-138 to Arg-
A	148, Arg-157 to Gly-163, Lys-165 to Asn-172.
710369	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 895 as
710007	residues: Asn-1 to Thr-10.
718826	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 896 as
710700	residues: Ser-57 to Pro-63, Lys-93 to Ser-99.
719790	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 897 as residues: Phe-4 to Gln-23, Glu-47 to Ala-56, Asn-95 to Gln-102, Gln-109 to Glu-115.
	Arg-168 to Glu-175, Thr-196 to Arg-201, Lys-209 to Asp-215, Val-236 to Val-243.
720222	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 898 as
120222	g referred ephopes include those comprising a sequence shown in SEQ 1D NO. 898 as

	residues: Glu-37 to Arg-43, Gly-62 to Pro-67. Gly-95 to Val-101, Gln-109 to Asp-114, Ala-137 to Phe-145. Asp-181 to Ser-188.
724033	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 899 as residues: Glu-55 to Glu-60, Asp-76 to Ser-85, Lys-106 to Asp-111, Gln-131 to Arg-
	137, Ala-172 to Gly-218.
724767	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 900 as
	residues: Lcu-49 to Tyr-56, Tyr-114 to Glu-136, Arg-142 to Gly-148.
727065	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 901 as
1	residues: Asn-41 to Gly-46, Lys-82 to His-88, Glu-107 to His-112, Leu-127 to Asp-
	132, Phe-163 to Phe-175, Thr-202 to Ilc-209, Lys-229 to Gly-237, Ala-239 to Tyr-245.
727246	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 902 as residues: Pro-2 to Gly-10.
739448	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 908 as
	residues: His-2 to Leu-8, Gln-33 to Glu-40, Ala-44 to Glu-55, Gly-57 to Ser-67, Glu-
	70 to Ala-84. Glu-95 to Lys-111, Ile-186 to Asp-205, Leu-232 to Asp-238.
740060	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 910 as
	residues: Pro-44 to Thr-50, Arg-72 to Lys-80, Tyr-241 to Asn-251, Lys-273 to Gly-
	282, Ser-302 to Asn-312. Pro-337 to Scr-343, Ile-367 to Asp-376, Gly-395 to Tyr-417,
	Ser-442 to Gln-448. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 911 as
741560	residues: Gln-33 to Tyr-39, Pro-42 to Phe-47.
742543	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 912 as
1	residues: Phe-10 to Tyr-15, Glu-139 to Asp-144, Glu-166 to Asn-171, Lys-175 to Glu-
	181.
742831	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 913 as
	residues: Val-64 to Glu-69.
745327	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 914 as
745695	residues: Arg-1 to Pro-13, Pro-54 to Ala-61. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 915 as
743093	residues: Trp-130 to Ser-135, Leu-199 to Thr-210, Ser-221 to Gln-229, Ala-249 to
	Tyr-255, Pro-257 to Pro-267, Ser-309 to Arg-314.
750316	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 916 as
	residues: Pro-18 to Asn-24, Thr-65 to Asp-70.
750522	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 917 as
	residues: Gln-10 to Lys-15.
750583	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 918 as
751000	residues: Lys-9 to Thr-15, Gln-32 to Gln-40. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 919 as
751020	residues: Arg-39 to Leu-47, Ser-107 to Ile-117, Pro-135 to Gin-144.
752196	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 920 as
732170	residues: Lys-20 to Lys-28.
753084	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 921 as
1	residues: Lys-84 to Thr-98, Arg-128 to Ser-134, Arg-244 to Asn-252, Lys-365 to His-
	372.
754957	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 922 as
	residues: Pro-101 to Glu-106, Glu-116 to Asp-127, Ser-199 to Ile-210, Asp-217 to
İ	Asp-229, Ser-239 to Gly-244, Gln-262 to Asn-273, Pro-279 to Ser-284, Lys-318 to
75/557	Arg-326, Lys-334 to Ile-341. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 923 as
756557	residues: Val-13 to Phe-21, Ile-55 to Pro-63, Ser-69 to Leu-74, Arg-82 to Leu-96, Asn-
	131 to Leu-139, Ile-156 to Thr-164, Thr-241 to Leu-249, Gly-273 to Ser-279, Thr-282
	to Arg-289.
756712	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 924 as
L	residues: Ile-4 to Thr-37, Gln-42 to Ser-48, Asn-56 to Lys-69, Ser-79 to Ser-85.
757414	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 925 as
	residues: Glu-14 to Thr-23, His-50 to Arg-62, Tyr-72 to Cys-78, Gly-121 to Pro-128.

757614	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 926 as
1	residues: Gly-13 to Cys-19. Thr-32 to Glu-38. Val-44 to Gln-53, Lys-55 to Asp-60,
	Gin-65 to Glu-70, Lys-89 to Glu-105, Glu-112 to Asp-142, Glu-147 to Arg-152, Glu-
1	211 to Leu-216, Leu-227 to Ser-232, Lys-245 to Lys-255, Glu-278 to Tyr-291, Gln-297
	to Arg-303.
759878	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 928 as
	residues: Trp-16 to Glu-21, Trp-45 to Pro-54. Ile-154 to Phe-162, Gly-174 to Leu-181.
760227	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 929 as
1	residues: Arg-99 to Asp-104.
766051	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 931 as
1 ,00031	residues: Asp-10 to Lys-19.
768053	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 933 as
1 700055	residues: Ile-1 to Tyr-7, Phe-52 to Cys-61, Val-118 to Ser-125.
768055	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 934 as
700055	residues: Asp-39 to Ser-46, Lys-92 to Lys-99, Val-165 to Phe-172, Lys-252 to Ala-
	261, Asn-268 to Ala-273.
760696	
769685	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 935 as
771020	residues: Pro-129 to Arg-135. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 936 as
771920	
1	residues: Pro-47 to Val-53, Asp-85 to Phe-97, Val-136 to Gly-144, Pro-166 to Glu-
	172, Leu-190 to Ser-197.
772790	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 937 as
1	residues: Leu-5 to Trp-13, Met-20 to Leu-39, Ile-50 to Pro-63, Glu-66 to Ser-72, Leu-
	112 to Gln-120, Ala-141 to Lys-146, Tyr-165 to Asp-173.
772916	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 938 as
	residues: Lys-16 to Arg-25.
773632	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 940 as
	residues: Arg-1 to His-33.
774364	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 941 as
	residues: Ser-97 to Asn-103.
775355	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 942 as
	residues: Ser-40 to Ala-46.
775844	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 943 as
	residues: Leu-20 to Ser-31, Thr-38 to Val-47.
777760	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 944 as
	residues: Thr-22 to Ser-28, Thr-35 to Glu-42, Met-47 to Thr-55.
779837	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 945 as
	residues: Thr-26 to Arg-31, Leu-75 to Lys-100.
780769	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 946 as
	residues: Gly-1 to Asp-7, Lys-25 to Lys-31, Tyr-65 to Gly-70, Thr-100 to Arg-106,
	Pro-118 to Glu-124, Lys-162 to Ser-172, Leu-176 to Leu-182.
781445	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 947 as
	residues: Asn-33 to Lys-38, Leu-67 to Met-73, Ser-111 to Lys-121, Lys-127 to Leu-
į	134, Pro-153 to Trp-158, Lys-237 to Met-249, Pro-280 to Tyr-292.
781531	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 948 as
1	
783018	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72.
783018	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as
783018	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-
	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85.
783018 783097	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 950 as
783097	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 950 as residues: Pro-1 to Asp-9, Pro-24 to Gly-40, Pro-47 to Thr-55, Gln-62 to Ser-76.
	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 950 as residues: Pro-1 to Asp-9, Pro-24 to Gly-40, Pro-47 to Thr-55, Gln-62 to Ser-76. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 951 as
783097 784198	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 950 as residues: Pro-1 to Asp-9, Pro-24 to Gly-40, Pro-47 to Thr-55, Gln-62 to Ser-76. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 951 as residues: Met-1 to Arg-15, Leu-43 to Glu-48, Asp-55 to Asp-62, Ser-111 to Lys-160.
783097	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 950 as residues: Pro-1 to Asp-9, Pro-24 to Gly-40, Pro-47 to Thr-55, Gln-62 to Ser-76. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 951 as residues: Met-1 to Arg-15, Leu-43 to Glu-48, Asp-55 to Asp-62, Ser-111 to Lys-160. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 952 as,
783097 784198	residues: Ala-8 to Pro-23, Gln-56 to Cys-61, Asn-66 to Pro-72. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 949 as residues: Asn-4 to Leu-17, Gly-19 to Phe-26, Pro-37 to Glu-43, Val-58 to Ser-64, Gln-80 to Gly-85. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 950 as residues: Pro-1 to Asp-9, Pro-24 to Gly-40, Pro-47 to Thr-55, Gln-62 to Ser-76. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 951 as residues: Met-1 to Arg-15, Leu-43 to Glu-48, Asp-55 to Asp-62, Ser-111 to Lys-160.

	Pro-194. Ser-206 to Cys-212, Ser-232 to Ala-246. Asp-293 to Ser-298.
785428	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 953 as
	residues: Arg-9 to Met-20, Glu-28 to Gly-33. Asn-49 to Lys-57, Thr-67 to Arg-75.
l	Ser-81 to Leu-87, Glu-103 to Thr-109, Pro-115 to Ile-120, Asn-146 to Ser-174, Ser-177
	to His-195, Met-197 to Ile-221, Asp-232 to Glu-240, Glu-289 to Phe-302, Cys-306 to
	Arg-314. Ser-357 to Scr-366, Lys-385 to Glu-401, Val-419 to Asp-427.
785845	Preferred epitopes include those comprising a sequence shown in SEQ 1D NO. 954 as
	residues: Arg-41 to Asp-52, Pro-82 to Arg-94, Pro-102 to Gln-107, Gln-170 to Tyr-
	181, Glu-248 to Lys-254. Asp-277 to Gly-287, Ala-302 to Arg-308, Thr-367 to Gly-
1	374.
785854	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 955 as
	residues: Asp-1 to Asp-17, Cys-59 to Asp-65.
787279	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 958 as
	residues: Lys-13 to Lys-20.
789002	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 959 as
	residues: Met-20 to Glu-29.
789008	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 960 as
	residues: Ser-24 to Arg-33, Ile-44 to Gly-57, Arg-63 to Asn-72, Ile-76 to Pro-82.
789555	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 961 as
	residues: Trp-106 to Thr-117, Trp-156 to Gln-163, Gln-173 to Asp-178, Gln-227 to
İ	Glu-233, Gln-255 to Glu-261, Glu-297 to Tyr-306, Thr-339 to Val-345, Leu-378 to Ile-
	385, Asp-414 to Lys-420, Cys-437 to Ile-444, Thr-491 to Gln-497, Glu-509 to Ser-515,
	Lys-526 to Glu-538.
789631	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 962 as
	residues: Thr-10 to Gly-18.
789779	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 963 as
1	residues: Glu-1 to Ala-13, Leu-103 to Ser-109.
790387	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 964 as
1	residues: His-1 to Ala-12.
790461	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 965 as
	residues: Glu-14 to Gly-23, Asp-47 to Met-53, Ala-55 to Thr-60, Pro-67 to Thr-73,
	Pro-78 to Gly-86, Tyr-91 to Pro-101, Ala-133 to Asn-139, Glu-169 to Gln-182, Glu-
	189 to Thr-195, Asn-197 to Arg-203, Gln-265 to Asp-271.
790931	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 966 as
	residues: Val-3 to Glu-13, Pro-29 to Pro-35, Glu-116 to Arg-125.
791176	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 967 as
	residues: Pro-1 to Pro-10, Pro-17 to Phe-28, Ser-61 to Pro-67.
792539	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 969 as
	residues: Ser-12 to Trp-17, Gln-20 to Lys-29, Asp-45 to Glu-51, Tyr-75 to Lys-83,
	Arg-103 to Gly-119, Gln-145 to Lys-155, Lys-166 to Leu-180, Thr-195 to Gly-203,
	Gln-209 to Val-219, Ser-222 to Ala-244, Leu-251 to Leu-260, Lys-277 to Lys-285.
792749	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 970 as
	residues: Ala-22 to Asp-41, Thr-61 to Met-66, Asp-191 to Lys-198, Arg-280 to Phe-
	287. Thr-289 to Lys-299, Pro-325 to Asp-332, Ser-351 to Arg-357.
793206	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 972 as
	residues: Gly-1 to Arg-6, Gln-11 to Arg-22, Glu-86 to Asp-91.
793626	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 974 as
,	residues: Ser-1 to Gly-13, Gly-17 to Asn-26.
794417	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 975 as
	residues: Ser-7 to Trp-16.
795197	Preferred epitopes include those comprising a sequence shown in SEO ID NO. 976 as
	residues: Ser-67 to Glu-73, Arg-129 to Gly-136, Phe-154 to Ala-161, Tyr-198 to Tyr-
	203, Pro-206 to Asp-212, Glu-222 to Cys-231.
795251	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 977 as
	residues: Phe-44 to Ser-50, Asp-57 to Pro-62, Asn-80 to His-90, Ser-110 to Ala-115,
	Ile-141 to Val-148, Glu-155 to Thr-173, Val-202 to Pro-217, Ile-221 to Val-229, Thr-

	233 to Ser-243, Val-253 to Thr-259, Ala-290 to Asn-320, Pro-322 to Ile-330, Ala-333
	to Mct-344. Val-362 to Lcu-367, Asp-397 to Val-402, Glu-422 to Gly-448, Met-453 to
	Gly-460.
795752	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 978 as
	residues: Pro-52 to Asn-63, Pro-70 to Ile-79, Arg-93 to Gln-111.
796261	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 979 as
i	residues: His-1 to Val-6, Cys-10 to Ser-15, Gly-26 to Ser-34, Trp-36 to Pro-58, Pro-96
	to Thr-102, Pro-111 to Tyr-116, Phe-131 to Gly-138, Pro-184 to Leu-190, Glu-237 to
	Gly-244, Pro-255 to Lys-267, Lys-271 to Leu-280.
796933	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 980 as
	residues: Arg-1 to Pro-14, Gln-47 to Cys-52, Asn-57 to Pro-63, Ser-277 to Lys-282.
799424	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 981 as
	residues: Tyr-18 to Leu-27, Mct-50 to Met-60, Leu-169 to His-178, Ser-233 to Ser-
	241.
799698	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 982 as
''''	residues: Pro-16 to Pro-21, Ala-54 to Glu-61, Ala-96 to Gly-105.
800351	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 983 as
	residues: Gly-21 to Gln-34, His-39 to Lys-53, Ser-63 to Tyr-71.
800573	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 984 as
	residues: Asp-33 to Arg-39, Ala-43 to Leu-48, Glu-256 to Gln-266, Gly-305 to Ile-
	311, Pro-314 to Ala-320, Gln-388 to Asn-394.
805815	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 985 as
******	residues: Arg-1 to Lys-22, Ser-34 to Arg-48, Thr-64 to Arg-70, Pro-81 to Phe-89, Arg-
	148 to Asn-154, Tyr-172 to Asp-185, Scr-205 to Asp-216, Tyr-278 to His-285, His-294
•	to Pro-299, Glu-326 to Gly-333, Gly-336 to Ser-345.
806445	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 986 as
	residues: Arg-15 to Gly-24, Lys-26 to Trp-32.
810309	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 987 as
	residues: Pro-33 to Phe-50, Ile-57 to Gly-62, Gln-72 to Asn-85, Ala-87 to Thr-172.
811022	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 988 as
	residues: Ala-1 to Met-11, Gln-62 to Trp-68, Ala-89 to Val-99.
811023	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 989 as
	residues: Tyr-54 to Lys-61, Met-64 to Thr-70.
811143	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 990 as
	residues: Ala-1 to Ser-7, Ser-19 to Gly-36, Arg-53 to Pro-58, Thr-87 to Glu-102, Arg-
	115 to Tyr-120, Thr-159 to Thr-164, Ala-171 to Ser-179, Ala-206 to Pro-217, Pro-224
	to Ala-233, Arg-253 to Ser-259.
813000	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 993 as
	residues: Tyr-25 to Lys-30, Lys-36 to Ile-43, Lys-52 to Gln-69, Glu-76 to Asp-81,
!	Arg-92 to Trp-104, Leu-120 to Lys-126, Ser-129 to Ser-135, Ser-139 to Thr-156, Pro-
	165 to Glu-178, Ser-181 to Thr-186, Tyr-196 to Lys-201, Cys-225 to Lys-230, Glu-234
	to Ser-242.
813431	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 995 as
	residues: Leu-23 to His-29, Pro-38 to Leu-46, Ser-59 to Gly-68, Pro-85 to Lys-108,
	Arg-119 to Phe-124, Ser-139 to Lys-156.
813450	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 996 as
	residues: Asn-1 to Trp-10.
813478	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 997 as
	residues: Ala-8 to Arg-14, Ile-64 to Thr-69, Val-94 to Asp-101, His-112 to Gln-117,
	Tyr-139 to Glu-145, Tyr-195 to Cys-208, Gly-216 to Gly-223, Asp-297 to Ser-307,
	Gly-378 to Leu-383, Ile-391 to Pro-404, Asn-451 to Ser-466.
813505	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 998 as
	residues: Thr-1 to Ala-20, Pro-22 to Lys-27, His-44 to Thr-51, Pro-53 to Thr-60, Arg-
	62 to Lys-79, Lys-97 to Asn-103, Pro-139 to Lys-144.
815552	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 999 as
	residues: Pro-1 to Ser-6, Pro-25 to Cys-31, Arg-142 to Lys-150.

815606	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1000 as residues: Arg-1 to Ala-11.
816048	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1001 as
010046	residues: Ala-13 to Thr-24, Glu-30 to Gln-39, Arg-69 to Gly-77, Gln-119 to Gly-126,
823981	[fyr-156 to Asn-162, Ser-184 to Gly-191.
023901	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1004 as
1	residues: Lys-1 to Cys-7, Ala-11 to Lys-17, Glu-90 to Ile-95, Asn-141 to Arg-148,
924264	Leu-158 to Ala-163, Ala-171 to Thr-177.
824364	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1005 as
	residues: Gln-43 to Gly-54.
824423	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1006 as
]	residues: Cys-33 to Arg-42, Val-53 to Met-63, Lys-71 to Lys-78, Gly-107 to Pro-118,
	Ala-159 to Leu-165, Val-272 to Arg-284, Pro-422 to Pro-427, Arg-437 to Gin-443,
	Ala-474 to Asp-482, His-519 to Cys-525, Ala-529 to Gln-535, Arg-540 to Gln-548.
825279	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1007 as
	residues: Ser-8 to Arg-14, Asp-23 to Gly-28, Ser-30 to Pro-37, His-52 to Ala-57, Pro-
22.5.10	65 to Scr-74. Pro-112 to Ser-118, Ala-181 to Pro-189.
825548	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1009 as
005505	residues: Pro-2 to Ser-9.
825725	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1010 as
	residues: Pro-1 to Gly-8, Leu-95 to Lys-100, Glu-118 to Thr-125, Ser-162 to Lys-167,
000000	Arg-201 to Tyr-206.
827079	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1012 as
	residues: Arg-9 to Ser-17.
827153	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1013 as
ł	residues: Val-32 to Ala-44, Pro-49 to Ser-57, Gln-77 to Gly-82, Asp-116 to Gly-127,
	Arg-165 to Asn-172.
827351	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1014 as
	residues: Gly-5 to Lys-11, Ser-59 to Lys-67, Glu-130 to Arg-136, Asn-176 to Leu-183.
827503	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1015 as
1	residues: Asp-61 to Val-67, Arg-113 to Asp-119, Ser-180 to Gly-191, Pro-199 to Ser-
ĺ	211, Ser-228 to Asn-238, Gly-276 to Ser-286, His-343 to Gly-351, Gln-354 to Arg-
	366, Leu-368 to Gln-382, Pro-393 to Ser-400, Asp-412 to Cys-418, Gly-430 to Leu-
0275.62	435, Gln-445 to Asp-450, Lys-484 to Val-491, Leu-513 to Gly-520.
827563	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1016 as
	residues: Pro-69 to Ala-81, Pro-84 to Gly-91, Ala-106 to Leu-112, Arg-216 to Lys-
027565	224, Trp-239 to Gly-250.
827565	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1017 as
	residues: Ala-1 to Ser-8, Ser-88 to Gly-96, Asn-121 to Asp-128, Cys-191 to Gly-196,
927902	Met-242 to Thr-248.
827893	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1018 as residues: Ser-41 to Ala-50, Glu-72 to His-77, Ala-120 to Glu-125, Thr-144 to Ile-153.
828072	Preferred epitopes include those comprising a sequence shown in SEO ID NO. 1019 as
020012	residues: Lys-30 to Leu-35.
828241	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1021 as
020241	residues: Gly-35 to Phe-45, Pro-47 to Arg-55, Glu-62 to Leu-70, Arg-102 to Tyr-111,
	Phe-128 to Gln-134, Val-139 to Met-144, Ser-180 to Gly-188, Lys-214 to Leu-219,
	Ser-241 to Glu-246, Phe-292 to Thr-298.
828287	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1022 as
020207	residues: Ala-12 to Thr-21, Ala-23 to Gly-31, Leu-43 to Gly-51, Lys-127 to Val-134.
828371	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1024 as
020371	residues: Gln-1 to Ala-6, Lys-50 to Pro-71, Pro-98 to Ser-111, Asp-148 to His-164,
	Asp-185 to Arg-191, Asp-238 to Gly-244, Pro-262 to Cys-274.
828403	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1025 as
020403	residues: Gly-1 to Trp-15, Arg-73 to Leu-82.
828501	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1026 as
020301	preferred ephopes include those comprising a sequence shown in SEQ ID NO. 1020 as

	residues: Arg-99 to Arg-105, Pro-171 to Ser-176, Lys-189 to Val-195, Lys-291 to Ala- 296.
828527	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1028 as residues: Glu-58 to Cys-63.
828538	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1029 as residues: Pro-9 to Thr-24, Thr-46 to Gly-52, Ser-70 to Thr-76, Ser-142 to Thr-149, Pro-154 to Ser-171, Glu-189 to Ser-196.
828541	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1030 as residues: Arg-9 to Pro-23, Gln-64 to Leu-69, Asp-76 to Asn-83, Lys-88 to Gln-93, Pro-129 to Thr-135, Gly-194 to Gly-203, Asp-223 to Gly-231, Thr-265 to Ile-281, Leu-287 to Lys-297.
828549	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1031 as residues: Pro-22 to Asn-28.
828562	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1032 as residues: Arg-26 to Asp-33, Asp-42 to Pro-58, Thr-63 to Lys-70, Thr-103 to Asp-114.
828576	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1033 as residues: Arg-11 to Gly-17. Pro-26 to Gly-31, Ala-48 to His-58.
828602	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1034 as residues: Tyr-1 to Met-8. Leu-10 to Lys-26, Pro-47 to Pro-54, Lys-128 to Ser-133.
828628	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1035 as residues: Thr-124 to Thr-129, Gly-136 to Phe-142, Asp-164 to His-171, Asp-180 to Tyr-194.
828684	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1037 as residues: Scr-16 to Thr-22, Arg-39 to Ala-51, Arg-60 to Gly-65, Thr-67 to Arg-90, Lys-109 to Gln-125, Scr-146 to Arg-159, Gln-166 to Thr-176, Glu-192 to Tyr-197, Val-267 to His-279, Ala-351 to Gly-356, Phe-363 to Gly-368, Gly-387 to Arg-392, Asp-488 to Ala-498.
828727	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1038 as residues: Gly-14 to Val-21, Asp-40 to Gln-57, Gln-86 to Tyr-93, Gln-98 to Asp-104, Lys-124 to Asp-130, Gln-138 to Cys-156, Tyr-170 to Gln-175, Gln-196 to Ala-201.
828734	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1039 as residues: Asp-5 to Trp-19, Ile-37 to Pro-42, Asp-52 to Asp-72, Glu-85 to Ser-92, Ser-107 to Leu-117, Asp-128 to His-147.
828842	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1041 as residues: Ala-25 to Phe-32, Glu-54 to Ser-61, Thr-74 to Glu-79, Glu-99 to Lys-105, Glu-112 to Glu-121.
828843	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1042 as residues: Pro-3 to Asn-11, Gln-46 to Ala-51, Asn-62 to Lys-74, Val-108 to Gln-113, Arg-119 to Gly-163, Ala-223 to Lys-237.
828851	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1043 as residues: Thr-3 to Lys-8, Leu-63 to Val-70, Lys-141 to Val-149, Ile-326 to Thr-333.
828856	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1044 as residues: Leu-1 to Gly-10.
828862	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1045 as residues: Pro-1 to Pro-9, Arg-81 to Glu-87, Gln-114 to Glu-119.
828870	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1046 as residues: Ser-1 to Gly-18, Trp-25 to Gly-31, Arg-46 to Ser-52, Ala-103 to Ala-108, Ser-154 to Gly-165, Gln-228 to Pro-236, Ser-284 to Gly-291, Ala-321 to Asp-327, Lys-377 to Asn-394, Asp-406 to Ser-416.
828873	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1047 as residues: Tyr-15 to Gly-20, Asn-72 to Asp-80, Pro-105 to Pro-110, Gln-149 to Arg-154, Glu-161 to Gly-167, Ile-312 to Asp-318, Lys-353 to Leu-361, Arg-379 to Thr-385, Pro-423 to Trp-435, Pro-437 to Cys-444, Asn-450 to Met-466.
828892	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1048 as residues: Asp-19 to Asn-25, Gly-67 to Glu-79.
828893	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1049 as

	residues: Ser-55 to Thr-60, Glu-97 to Ser-103, Thr-164 to Glu-170, Gly-192 to Gly-
	197, Leu-204 to Ser-218, Ala-238 to Ser-250, Asp-265 to Tyr-292, Gly-298 to Gly-
	307, Gly-351 to Met-359, Phe-389 to Glu-400.
828897	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1050 as
<u></u>	residues: Phe-28 to Arg-33.
828910	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1051 as
	residues: His-1 to Ile-13, Arg-20 to Glu-64, Arg-83 to Gln-89. Tyr-145 to Asp-152.
828927	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1052 as
	residues: Glu-10 to Pro-21, Thr-54 to Gly-60, Cys-79 to Glu-90, Lys-154 to Lys-159.
828932	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1053 as
	residues: Arg-1 to Arg-9, Phe-54 to Pro-60, Gln-74 to Gly-90, Asn-114 to Gly-119,
į	Cys-124 to Ser-132, Thr-139 to Leu-151, Asp-171 to Lys-182, Ala-188 to Leu-193,
l	Val-203 to Trp-222, Lys-230 to Glu-236, Glu-244 to Asp-250, Leu-258 to Gly-268,
<u></u>	Gly-283 to Asp-288, Ser-291 to Trp-297, Gly-300 to Ala-308.
828933	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1054 as
	residues: Glu-21 to Ser-34, Thr-130 to Tyr-138.
828941	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1055 as
ļ	residues: Gly-1 to Ala-6, Pro-15 to Gly-22, Asn-160 to Gln-177, Asn-193 to Asp-199,
	Glu-205 to Leu-211.
828963	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1057 as
	residues: Pro-48 to Gly-54, Ser-56 to Ser-76, Lys-102 to Pro-107, Ser-146 to Gly-153,
939064	Ser-208 to Arg-213, Tyr-285 to Leu-299, Pro-314 to Phe-319, Asn-322 to Asn-327.
828964	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1058 as
929066	residues: Thr-36 to Cys-47.
828966	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1059 as residues: Gly-1 to Ser-16, Met-26 to Pro-31, Lys-128 to Glu-134, His-165 to Gln-170,
1	Asp-207 to Asn-216, Pro-348 to Arg-359, Lys-433 to Ala-439, Gly-448 to Tyr-457.
828967	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1060 as
020907	residues: Met-135 to Arg-141, Gly-149 to Lys-166, Ile-188 to Ser-196, Gly-203 to
	Tyr-213, Gln-267 to Asp-278, Arg-298 to Trp-317, Leu-319 to Leu-326, Gln-344 to
	Thr-349, Pro-410 to Ser-419, Ala-500 to Ala-510.
828977	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1061 as
	residues: Gly-32 to Tyr-42, Asn-52 to Glu-58, Ser-78 to Gly-87, Lys-97 to Gly-109,
i	Glu-116 to Arg-127, Pro-147 to Pro-152, Pro-162 to Asn-171, Leu-179 to Glu-185, Ile-
	203 to Glu-208, Val-222 to Gln-228.
828978	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1062 as
	residues: Asp-24 to Lys-30, Arg-49 to Lys-62, Arg-121 to Thr-149, Gly-163 to Leu-
	171, Ala-186 to Glu-195, Glu-216 to Ser-221, Ile-229 to Ser-236, Lys-258 to Lys-264,
	Lys-305 to Arg-313.
829001	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1064 as
	residues: Thr-11 to Cys-24, Arg-48 to His-55, Arg-62 to Gly-70.
829003	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1065 as
	residues: Lys-14 to Gly-22, Ser-61 to Asp-66, Cys-80 to Lys-91, Lys-97 to Arg-107,
	Gly-135 to Asn-146, Lys-198 to Lys-208, Met-221 to Thr-227, Phe-244 to Gly-256,
	Asp-292 to Gln-300.
829016	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1066 as
	residues: Arg-1 to Asp-11, Ala-17 to Gln-25, Glu-30 to His-37, Cys-39 to Thr-44,
00000	Asn-86 to Phe-93.
829027	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1067 as
000000	residues: Pro-1 to Ser-7, Thr-45 to Leu-63, Arg-113 to Thr-118, Pro-172 to Gly-182.
829028	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1068 as
	residues: Ser-I to Gln-19, Gly-32 to Phe-39, Ala-95 to Arg-116, Lys-122 to Glu-142,
	Ile-148 to Asn-156, Ser-168 to Asn-191, Ala-196 to Thr-204, Ser-289 to Lys-304, Leu-
920024	308 to Ser-314, Thr-332 to Ile-341. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1070 as
829034	residues: Ser-32 to Ala-43, Thr-62 to Glu-69, Phe-128 to Thr-156, Thr-179 to His-188,
	jesiuues. Sei-32 to Aia-43, Tiii-02 to Giu-03, Fiie-126 to Tiii-130, Tiii-179 to His-188,

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	Gly-196 to Glu-203. Pro-205 to Ala-219, Gln-221 to Ile-230, Pro-246 to Thr-255, Thr-
	271 to His-276. Asn-324 to Thr-344, Pro-364 to Ala-370, Tyr-427 to Arg-434, Gly-440
	to Pro-445.
829036	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1071 as
	residues: Leu-16 to Phe-21, Thr-69 to Lys-74, Asn-87 to His-92, Thr-126 to Leu-137.
	Phe-154 to Lys-164, Ala-171 to Asp-178, Ile-192 to Thr-203, Glu-261 to Ser-273.
829049	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1072 as
	residues: Gly-50 to Tyr-59.
829073	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1073 as
	residues: Asn-1 to Met-6, Asn-26 to Ser-35, Pro-43 to Ile-54.
829075	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1074 as
	residues: Gly-14 to Pro-30, Ser-64 to Ser-69, Asn-97 to Arg-109.
829076	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1075 as
	residues: Lys-84 to Gly-94, Asn-142 to Ile-147.
829080	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1076 as
	residues: Gly-13 to Trp-23, Pro-39 to Gly-44.
829087	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1077 as
	residues: Pro-13 to Arg-24.
829095	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1079 as
000110	residues: Pro-8 to Pro-13.
829118	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1081 as residues: Arg-7 to Val-12, Ile-52 to Thr-70, Ser-86 to Asp-91, Thr-126 to Ser-138.
020162	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1082 as
829152	
920160	residues: Asp-12 to Ser-19. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1083 as
829160	residues: Ala-7 to Arg-20.
829163	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1084 as
027103	residues: Ser-23 to Asp-32, Val-36 to Glu-59, Ser-65 to Asn-76, Cys-91 to Ser-102,
	Pro-108 to Leu-115, Thr-151 to Gin-164, Glu-167 to Lys-176.
829176	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1085 as
	residues: His-1 to Asn-8, Cys-22 to Arg-27, Gly-34 to Ser-44, Tyr-60 to Ser-65, Ser-
1	118 to Gln-123, Ser-149 to Trp-154, Pro-159 to Gly-168, Gln-207 to Leu-220.
829204	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1086 as
	residues: Ala-11 to Ser-19, Thr-104 to Lys-133.
829207	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1087 as
}	residues: Lys-5 to Ser-11, Pro-31 to Ser-37, Pro-87 to Asp-92, Asp-115 to Lys-123,
	Ser-149 to Arg-155, Thr-243 to Pro-253.
829228	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1088 as
·	residues: Pro-1 to Trp-6, Leu-73 to Tyr-79, Glu-108 to Thr-117, Asp-136 to Asp-142,
	Ser-201 to Pro-207, Leu-224 to Pro-233, Val-242 to Ala-248, Ser-312 to Leu-319, Val-
İ	349 to Ser-359, Ala-362 to His-368, Thr-370 to Gly-376, Lys-403 to Tyr-409, Glu-426 to Arg-431, Lys-455 to Asp-460, Arg-499 to Thr-505, Asp-561 to Ser-570, Ser-665 to
	Ser-673.
829252	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1089 as
027232	residues: Thr-9 to Val-16.
829269	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1091 as
02,7203	residues: Ser-1 to Glu-7, Lys-76 to Gln-83.
829277	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1092 as
02/2//	residues: Lys-88 to Phe-97, Thr-106 to Leu-120, Thr-147 to Pro-152, Pro-173 to Met-
	179.
829290	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1093 as
	residues: Pro-1 to Pro-19, Pro-25 to Lys-30.
829308	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1096 as
	residues: Met-26 to Asn-37, Glu-42 to Gln-51, Thr-68 to Ser-95, Ala-97 to Lys-113,
	Asp-156 to Val-161, Val-208 to Asp-215, Pro-217 to Ala-228.
829349	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1097 as

	residues: Asn-18 to Lys-24, Asp-87 to Asn-94, Glu-116 to Gly-125.
829354	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1098 as
	residues: Ala-1 to Asn-16. Pro-36 to Arg-43.
829388	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1099 as
}	residues: Glu-91 to Pro-100, Tyr-122 to Thr-127, Thr-168 to Val-173. Thr-210 to Asp-
<u> </u>	215. Leu-219 to Gly-224. Gly-232 to Val-237.
829626	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1101 as
	residues: Gly-145 to Ala-151.
829730	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1102 as
	residues: Pro-22 to His-27, Pro-87 to Asp-93, Arg-109 to Lys-115, Arg-172 to Glu-
	177, Glu-219 to Asp-226.
829892	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1103 as
	residues: Tyr-36 to Ala-46, Val-58 to Asn-63, Glu-73 to Asn-78, Asn-90 to Asn-95,
	Ser-125 to Leu-133, Glu-143 to Pro-150, Phe-186 to Leu-191, Lcu-274 to Glu-281,
1	Lys-303 to Phe-308. Thr-323 to Gly-330.
829938	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1105 as
i	residues: Thr-1 to Pro-14, Ser-36 to Thr-57, Ser-81 to Thr-91, Glu-103 to Leu-110,
	Glu-124 to Tyr-130, Ala-135 to Lys-140, Leu-146 to Glu-162, Lys-167 to Glu-172,
	Glu-199 to Val-213.
829969	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1106 as
	residues: Arg-12 to His-21, Arg-77 to Scr-88.
829982	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1107 as
	residues: Arg-6 to His-14, Ser-40 to Met-47, Thr-68 to Cys-74, Ile-97 to His-115, Gly-
	118 to Pro-124.
830007	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1108 as
050007	residues: Ala-7 to Ala-16.
830019	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1109 as
650015	residues: Leu-21 to Pro-27.
830073	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1110 as
830073	residues: Gly-16 to Val-22, Pro-45 to Lys-50, Phe-58 to Arg-65, Ser-135 to Gly-141,
	Gly-153 to Ser-158, Pro-160 to Tyr-168.
830148	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1114 as
030140	residues: Asp-63 to Lys-81, Gly-101 to Gly-108, Pro-182 to Ala-200, Pro-210 to Met-
ļ	216, Pro-235 to Gly-243.
830183	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1117 as
630163	residues: Pro-29 to Lys-37, Pro-40 to Val-47, Tyr-62 to His-67.
920104	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1118 as
830194	residues: Ala-43 to Lys-51, Glu-66 to Leu-74, His-81 to Glu-88, Arg-98 to Ser-105,
1	Gly-111 to Gln-116, Leu-166 to Lys-182, Leu-261 to Ala-273, Glu-294 to Arg-302,
1	
930307	Glu-335 to Asp-347. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1119 as
830207	residues: Pro-14 to Pro-48, Asp-55 to Gly-61, Lys-94 to Asn-99, Ala-107 to Ser-115,
	lle-117 to Asn-124, Thr-133 to Cys-139, Thr-142 to Ile-147, Gly-163 to Ser-169.
930343	
830242	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1120 as
1	residues: Glu-29 to Lys-34, Leu-151 to Gln-157, Arg-160 to Ser-171, Gln-177 to Pro-
	190.
830328	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1121 as
	residues: Pro-18 to Met-24, Glu-66 to Gln-78, Ala-85 to Arg-93, Glu-99 to His-108,
	Leu-114 to Asp-137, Pro-171 to Gln-176, Gly-205 to Leu-213.
830340	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1122 as
	residues: Gly-12 to Lys-18, Arg-46 to Glu-56, Leu-67 to Gly-73, Ala-91 to Tyr-112.
830341	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1123 as
	residues: Leu-14 to Gln-20, Asn-34 to Glu-41, Lys-193 to Asn-198.
830351	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1124 as
	residues: Pro-1 to Leu-13, Gly-42 to Pro-51, Arg-64 to Ala-69, Met-104 to Asp-109,
	Cys-125 to Trp-132, Asp-161 to Trp-175, Glu-206 to Glu-218.

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830358	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1125 as residues: Cys-75 to Thr-81.
830400	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1127 as
""	residues: Pro-1 to Gly-6, Arg-17 to Arg-33, Glu-151 to Trp-157, Ile-187 to Tyr-193.
1	Lys-249 to Glu-258, Asn-289 to Ser-294, Pro-340 to Lys-353.
830437	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1128 as
830437	
	residues: Ala-87 to Ser-94, Asp-104 to Arg-112, Leu-114 to Asp-119, Ser-186 to Thr-
030466	202.
830466	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1130 as
020105	residues: Pro-14 to Ile-24, Thr-35 to Phe-42, Ser-45 to Asn-57, Pro-65 to Trp-89.
830497	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1131 as
	residues: Thr-1 to Leu-9. Ser-46 to Leu-56, Glu-117 to Lys-124, Pro-129 to Asp-135,
	Ala-144 to Gln-150, Gly-156 to Lys-162, Phe-182 to Pro-187, Pro-196 to Gln-201,
	Lys-217 to Asp-227.
830511	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1132 as
	residues: Lys-13 to Cys-44, Lys-101 to Arg-109, Gln-120 to Gly-129.
830540	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1135 as
	residues: Leu-31 to Lys-37, Arg-48 to Asn-54.
830550	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1136 as
	residues: Pro-8 to Cys-15, Val-80 to Cys-85.
830567	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1137 as
	residues: Lys-28 to Leu-33, Pro-60 to Ser-66.
830586	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1138 as
1	residues: Pro-1 to Gln-15, Arg-33 to Leu-40, Arg-72 to Ser-78, Leu-98 to Asp-103,
•	Phe-116 to Gly-124, Pro-152 to Arg-158, Thr-193 to Pro-200, Leu-213 to Phe-219,
	Asp-229 to Lys-237, Lys-246 to Lys-258, Arg-275 to Thr-280, Thr-306 to Lys-312,
	Leu-320 to Arg-328, Ala-335 to Asn-340, Gly-342 to Trp-349, Cys-364 to Pro-372.
830632	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1139 as
	residues: Ala-6 to Thr-14, Arg-143 to Lys-148.
830659	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1142 as
	residues: Thr-32 to Tyr-40, Ala-67 to Gln-82, Arg-128 to Thr-133, Leu-137 to Thr-
<u> </u>	146, Pro-187 to Ser-193.
830696	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1143 as
	residues: Glu-83 to Lys-91.
830743	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1145 as
	residues: Pro-11 to Phe-16, Thr-48 to Ser-60.
830770	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1146 as
	residues: Thr-36 to Thr-44.
830830	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1147 as
1	residues: Lys-73 to Thr-78, Pro-84 to Pro-96, Lys-107 to Glu-124, Ile-142 to Cys-153,
	Asp-179 to Asn-184.
830838	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1148 as
ļ	residues: Ser-17 to Arg-22, Gly-48 to Val-56, Asn-217 to Asp-223, Thr-238 to Asn-
	243.
830851	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1149 as
	residues: Arg-1 to Val-7, Ala-156 to Phe-162, Arg-216 to Lys-239.
830856	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1151 as
<u> </u>	residues: Trp-29 to Gly-35, Thr-41 to His-47, Val-95 to Lys-111.
830862	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1152 as
1	residues: Arg-14 to Val-22, Ala-24 to Gly-35, Arg-37 to Lys-58, Ala-88 to Ala-94,
<u> </u>	Lys-164 to Ser-172.
830879	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1153 as
ľ	residues: Cys-34 to Leu-44, Ser-60 to Gly-69, Asp-118 to Gly-123, Cys-148 to Gln-
	154.
830919	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1154 as
L	residues: Pro-1 to Ser-41, Arg-53 to Pro-61, Arg-66 to Gln-132.

830969	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1155 as residues: His-17 to Pro-27, Phe-31 to Val-38, Gly-53 to Thr-62.
830991	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1156 as
000777	residues: Arg-1 to Pro-14, Ala-44 to Ser-56, His-69 to Lys-75, Gly-89 to Lys-98, Tyr-
1	101 to Tyr-121. Pro-123 to Thr-131. Pro-149 to Gly-171, Tyr-186 to Glu-192.
831002	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1157 as
03.002	residues: Glu-63 to Asn-73, Pro-114 to Tyr-122. Ser-194 to Glu-201, Ile-263 to Ser-
į	269.
831003	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1158 as
00.000	residues: Ile-9 to Leu-17, Asp-63 to Gly-70, Leu-112 to Ala-128.
831021	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1159 as
	residues: Asn-6 to Asp-12.
831036	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1160 as
	residues: Ser-6 to Ser-25, Tyr-37 to Lys-42, Arg-49 to Tyr-54, Pro-56 to Glu-61, Gln-
ľ	72 to Cys-77, Lys-104 to Glu-110, Lys-134 to Met-142, Asp-147 to Arg-158, Arg-189
	to Asn-194.
831071	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1161 as
	residues: Thr-41 to Arg-49, Glu-137 to Asp-142, Tyr-158 to Glu-163, Arg-184 to Thr-
	199, Arg-239 to Gly-253, Pro-297 to Gly-304, Pro-319 to Ile-327, Leu-347 to Val-356,
	Asn-435 to Leu-441, Asp-443 to Ser-452, Ala-457 to Thr-462, Asp-479 to Arg-484,
	Gly-510 to His-516, Glu-555 to Thr-565, Asp-597 to Ser-602, Thr-615 to Asp-622,
	Val-653 to Leu-661, Ala-684 to Arg-697, Ser-704 to Glu-712, Ala-731 to Ala-737,
021000	Lys-800 to Met-805.
831099	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1163 as
	residues: Leu-12 to Gly-18, Leu-93 to Ile-98, Lys-165 to Ser-183, Thr-198 to Lys-211,
	Glu-232 to Gly-237, Pro-239 to Gly-249, Arg-257 to Asp-278, Cys-292 to Glu-297, Arg-306 to Ser-316, Asp-323 to Asn-331, Glu-347 to Gly-354, Thr-365 to Asn-370,
•	Pro-390 to Thr-396, Asn-420 to Ser-433, Val-440 to Gln-451, His-457 to Asn-465,
1	Phe-533 to Met-538, Ala-540 to Tyr-550, Pro-560 to Lys-565.
831113	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1164 as
1	residues: Ser-26 to Arg-33, Pro-51 to Thr-56, Cys-82 to Asp-94, Pro-104 to Gly-128.
831120	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1165 as
	residues: Ala-39 to Leu-47, Val-49 to Lys-55, Thr-66 to Asp-75, Thr-85 to Gly-104,
	Ala-114 to Gly-147, Pro-176 to Thr-199, Ser-205 to Ser-221, Glu-233 to Lys-240, Lys-
l	246 to Asp-251, Glu-256 to Ser-267, Ser-291 to Leu-302, Thr-305 to Asp-324, Cys-336
	to Val-345, Phe-367 to Cys-375.
831172	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1166 as
l	residues: Pro-1 to Gly-7, His-119 to Gly-125, His-145 to Asp-151, Leu-173 to Leu-
	178.
831178	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1167 as
021104	residues: Glu-37 to Asn-42, Ser-48 to Thr-54, Pro-101 to Glu-106.
831184	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1168 as
831203	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1169 as
. 651205	residues: Thr-1 to Ser-6, Leu-10 to Asn-23, Gln-31 to Arg-36, Arg-43 to His-49, Ala-
1	58 to Leu-63, Gln-81 to Asp-105, Glu-113 to Ile-122, Pro-132 to Lys-137, Scr-175 to
ŀ	Gln-181.
831257	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1173 as
331.257	residues: Arg-87 to Leu-96, His-104 to Lys-112, Asp-144 to Pro-150.
831277	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1174 as
	residues: Arg-1 to Gly-13.
831317	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1175 as
	residues: Ser-97 to Lys-102, Thr-108 to Gly-119, Lys-151 to Gly-157, Pro-204 to Glu-
	210, Gln-224 to Gly-230, Val-238 to Cys-245, Met-279 to Asn-284, Gly-332 to Glu-
	349.
831339	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1176 as

	residues: Met-1 to His-19, Pro-21 to Pro-27, Ala-49 to Gly-59, Pro-82 to Ala-104.
831363	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1177 as
	residues: Thr-1 to Ser-14, Thr-82 to Pro-89, Mct-102 to Ala-109, Phe-117 to Ile-124,
	Asp-142 to Arg-148, Thr-196 to Trp-205, Gln-304 to Leu-310, Gln-325 to Ser-331,
	Gly-387 to Thr-393, Ala-415 to Lys-430, Pro-469 to Pro-477, Gly-500 to Ile-506, Arg-
	521 to Gly-529. Pro-534 to Gly-541, Gln-553 to Lys-558, Ala-571 to Glu-579.
831385	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1180 as
05.005	residues: Ser-1 to Thr-9, Ala-32 to Asn-37, Thr-40 to Tyr-49, Gln-71 to Thr-80.
831390	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1181 as
031370	residues: Trp-50 to Gly-55, Leu-109 to Val-119, Phe-146 to Asp-158, Ser-165 to Trp-
	172. Phe-192 to Ile-197, Leu-241 to Asp-252, Lys-268 to Pro-273, Ser-310 to Lys-315,
	Asp-334 to Ala-342. Pro-348 to Tyr-353.
831391	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1182 as
631391	
	residues: Ser-28 to Pro-38, Pro-45 to Cys-55, Leu-70 to Ser-77, Glu-98 to Phe-104,
221425	Asp-112 to Ser-122, Thr-152 to Lys-158.
831405	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1183 as
	residues: Asp-47 to Ser-55, Glu-86 to Cys-95, Glu-105 to Gly-113, Gln-133 to Asn-
	138. Arg-144 to Asp-156.
831476	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1185 as
	residues: Gln-28 to Gly-33, Asp-41 to Trp-47, Asn-51 to Ser-56, Ser-73 to Asn-83,
	Trp-111 to Asn-117, Leu-133 to Gln-138, Arg-143 to Tyr-150, Thr-156 to Glu-165.
831488	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1186 as
	residues: Glu-53 to Asn-59, Lys-97 to Phe-104, Lys-133 to Ala-138.
831519	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1188 as
	residues: Ser-17 to Gly-25, Thr-47 to Leu-59, His-71 to Arg-77, Pro-83 to Gln-90,
	Tyr-133 to Ser-143, Arg-160 to Gly-169, Pro-188 to Val-193, Glu-202 to Glu-208,
	Leu-283 to Arg-288, Glu-295 to Leu-301, Ala-327 to Leu-333, Ala-426 to Pro-433,
	Leu-444 to Leu-456, Asn-492 to Ala-498.
831550	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1190 as
	residues: Arg-1 to Gly-15, Ser-42 to Trp-51, Pro-59 to Arg-64.
831560	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1191 as
	residues: Arg-58 to Asp-64.
831570	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1193 as
}	residues: Thr-61 to Cys-74, Gly-92 to Cys-104, Cys-128 to Ser-133, Asn-179 to Gly-
	186, Ser-198 to Cys-226, Asn-265 to Ser-274, Ser-280 to Ile-285, Ser-291 to Asp-297,
	Leu-305 to Gly-315, Phe-317 to Gly-333, Asp-336 to Leu-344, Phe-354 to Cys-361.
831596	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1195 as
	residues: Gln-80 to Gly-85.
831627	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1196 as
	residues: Arg-1 to Ser-12, Gly-94 to Thr-106, Ser-161 to Leu-169, Ser-183 to Val-188,
	Glu-199 to Cys-205, Ser-246 to Ile-251, Leu-271 to Thr-276.
831649	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1197 as
	residues: Tyr-32 to Lys-39.
831664	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1198 as
	residues: Lys-1 to Asp-42, Arg-71 to Ala-76, Gln-138 to Phe-145, Lys-170 to Thr-178,
	Cys-186 to Asp-192.
831684	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1200 as
05.007	residues: Ile-135 to Ala-140, Tyr-151 to Asn-157, Ser-183 to Ile-190, Gly-196 to Lys-
	201, Lys-226 to Lys-232, Asn-246 to Thr-252, Asp-293 to Gly-300.
831687	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1201 as
031007	residues: Ala-56 to Tyr-63.
831726	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1202 as
051720	residues: Arg-3 to Arg-15, Lys-34 to Thr-39, Asn-41 to Lys-59, Ala-104 to Glu-110.
831762	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1204 as
001/02	residues: Pro-83 to Leu-91, His-116 to Ala-122, Pro-141 to Ser-155.
921040	
831848	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1206 as

	residues: Gln-16 to Thr-23.
831861	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1207 as
	residues: Ala-20 to Lys-26, Pro-59 to Pro-67, Ser-104 to Thr-121, Gln-130 to Gln-136.
831866	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1208 as
1	residues: Arg-11 to Ala-24, Ile-39 to Lys-45, Arg-76 to Pro-85. Lys-124 to Lys-130,
	Pro-139 to Ser-153. Ala-156 to Glu-170, Ser-179 to Thr-184, Asp-234 to Gly-244, Gly-
Į.	321 to Lys-329.
831899	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1210 as
1	residues: Asp-11 to Trp-16, Pro-37 to Thr-44, Pro-74 to Pro-82, Arg-112 to Gln-119,
	Cys-126 to Arg-138, Arg-199 to Thr-204.
831913	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1211 as
	residues: Pro-22 to Cys-27, Glu-54 to Glu-60, Asp-112 to Phc-117, Lys-183 to Asp-
	189, Gln-277 to Tyr-282, Pro-325 to Arg-331, Gly-336 to Tyr-346.
831985	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1213 as
051705	residues: Cys-7 to Asp-12, Pro-21 to Gly-26.
831986	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1214 as
651760	residues: Cys-1 to Scr-7. Ala-62 to Gly-72, Pro-83 to Ala-101.
922010	
832010	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1215 as
	residues: Leu-1 to Lys-21, Glu-39 to Cys-47, Lys-49 to Gln-61, His-64 to Gly-76, Thr-
922016	83 to Lys-90, His-92 to Ile-99. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1216 as
832016	
	residues: Phe-28 to Asn-33, Leu-55 to Tyr-80, Pro-126 to Gly-132, Pro-162 to Gly-
	169, Pro-194 to Arg-201.
832041	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1217 as
l	residues: Lys-55 to Met-63, Arg-120 to Asp-132, Gly-266 to Glu-281, Val-313 to Thr-
 _	319, Leu-361 to Ser-370, Tyr-406 to Met-412, Leu-465 to Trp-470.
832049	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1219 as
	residues: Leu-80 to Lys-87, Lys-102 to Thr-109, Glu-195 to Thr-200, Thr-203 to Asp-
`	209.
832122	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1220 as
	residues: Asn-29 to Phe-36, Asp-41 to Ser-50.
832197	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1222 as
L	residues: Glu-61 to Leu-70.
832237	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1223 as
	residues: Lys-28 to Val-35, Arg-41 to Arg-55, Pro-76 to Thr-87.
832246	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1224 as
ĺ	residues: Arg-17 to Asn-23, Arg-90 to Gly-95, Leu-114 to Glu-121, Pro-153 to Asp-
	158.
832256	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1225 as
	residues: Gly-15 to Asn-22.
832280	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1226 as
1	residues: Glu-1 to Trp-16, Ala-32 to Glu-38, Ala-49 to Gln-55, Pro-61 to Gln-66, Ala-
	78 to Asp-100, Leu-107 to Thr-127, Pro-133 to Phe-157, Pro-160 to Thr-171, Leu-179
l	to Asp-196, Asp-201 to Lys-222, Pro-249 to Ile-254, Val-258 to Val-263, Thr-268 to
ł	Ser-277, Thr-279 to Ala-295, Gly-299 to Phe-327, Val-335 to Asp-346, Lys-366 to
	Asp-378.
832285	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1227 as
	residues: Phe-18 to Leu-23.
832294	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1228 as
	residues: Pro-21 to Gln-28, Pro-56 to Leu-64, Glu-79 to Pro-95, Met-125 to Gly-138.
832326	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1229 as
052520	residues: Ser-30 to Trp-45, Gln-64 to Cys-72, Pro-74 to Pro-80, Ala-92 to Arg-98, Trp-
	104 to Ser-112, Ser-129 to Asp-135, Pro-145 to Gln-152, Arg-168 to Gly-173, Gln-176
	to Pro-183.
832370	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1232 as
052570	residues: Ala-5 to Ala-11, Pro-23 to Pro-36, Glu-72 to Gly-82, Pro-85 to Pro-91, Asp-
	residuees. Ata-5 to Ata-11, 110-25 to 110-50, Ota-12 to Oly-02, 110-03 to 110-91, ASp-

	98 to Gly-119, Pro-121 to Glu-127.
832381	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1233 as
	residues: Arg-1 to Glu-6, Arg-52 to Ala-58, Phe-72 to Leu-79, Gly-88 to Glu-93, Tyr-
L	124 to Arg-134.
832454	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1235 as
L	residues: Ala-23 to Asp-41.
832465	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1236 as
ļ	residues: Ala-1 to Gly-7, Ala-32 to Val-45. Ile-65 to Ser-75, Ser-93 to Ser-108.
832475	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1237 as
	residues: Arg-1 to Val-10, Thr-65 to Ser-71, Arg-83 to Tyr-96, Trp-104 to Trp-111.
832495	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1238 as
020400	residues: Arg-9 to Arg-14.
832498	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1239 as
	residues: Pro-26 to Asp-31, Thr-113 to Gly-125, Asn-158 to Glu-163, Asn-288 to Val-
000001	293.
832501	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1240 as
022505	residues: Ser-8 to Glu-13.
832505	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1241 as
	residues: Ala-27 to Arg-46, Pro-54 to Arg-76, Arg-134 to Lys-140, Asn-148 to Ser-
832554	154, Lvs-166 to Thr-172. Pro-175 to Gln-182, Asp-185 to Asp-192.
832334	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1243 as
922560	residues: Arg-26 to Val-31, Asn-122 to Thr-128.
832569	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1244 as
022570	residues: Gln-6 to Met-16.
832578	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1245 as residues: Arg-15 to Leu-27, Ser-62 to Gly-72, Pro-107 to His-112, Pro-122 to Gln-142,
	Glu-147 to Arg-158, Lys-177 to Lys-191, Leu-195 to Val-202, Leu-206 to Pro-218,
	Glu-228 to Gln-233, Asp-239 to Asp-244, Glu-258 to Gln-278.
832615	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1246 as
052015	residues: Gln-41 to Ala-48.
832632	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1248 as
	residues: Asn-60 to Val-70, Glu-93 to Trp-107, Arg-116 to Gln-125, Leu-133 to Lys-
	141, Lys-162 to Glu-167.
832633	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1249 as
	residues: Gly-8 to Trp-13, Pro-36 to Gly-41, Pro-91 to Ala-96.
834859	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1252 as
	residues: Tyr-16 to Leu-22, Asp-24 to Asp-34, Gly-43 to Ala-48, Gly-57 to Thr-68,
	Gly-118 to Ser-127, Ile-129 to Tyr-134, Pro-139 to Asp-162.
834861	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1253 as
	residues: Glu-14 to Glu-50, Glu-67 to Asp-74, Leu-89 to Asn-95.
834890	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1254 as
	residues: Arg-8 to Lys-13, Gly-35 to Lys-42, Ala-48 to Lys-54, Ala-105 to Leu-110,
	Gly-150 to Val-157, Phe-164 to Asn-173.
835079	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1255 as
	residues: Ser-53 to Pro-60.
835554	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1256 as
	residues: Ile-31 to Ile-38, Asp-116 to Arg-121, Phe-246 to Leu-251, Lys-280 to Tyr-
	291, Met-363 to Arg-373, Gly-381 to Trp-386.
835723	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1258 as
	residues: Glu-20 to Thr-26, Trp-47 to Ser-57, Pro-98 to Asn-105, Pro-124 to Phe-129,
	Ala-173 to Val-183, Lys-190 to Ser-196, Asn-277 to Asn-284, Glu-297 to Phe-306,
•	Thr-322 to Lys-327, Gln-372 to Val-383, Pro-387 to Gly-395. Ser-406 to Thr-415, Arg-
	432 to Thr-442.
835791	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1259 as
00.50:-	residues: Ala-4 to Gly-10.
835817	Preferred epitopes include those comprising a sequence shown in SEQ 1D NO. 1260 as

	residues: Glu-37 to Leu-43.
835840	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1261 as
	residues: Gln-1 to Asn-6, Pro-18 to Ile-31.
836048	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1262 as residues: Lys-1 to Lys-11, Tyr-27 to Glu-35, Glu-61 to Gly-68.
836898	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1263 as
	residues: Gln-94 to Lys-102, Gly-140 to Thr-154, Arg-173 to Asp-196, Thr-201 to
	Asp-206, Glu-241 to Gly-248.
836927	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1264 as
	residues: His-1 to Arg-12.
837344	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1265 as
L	residues: Pro-15 to Ile-24.
837789	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1266 as
	residues: Ser-1 to Trp-7, Asp-47 to Ile-52, Pro-70 to Ser-80, Cys-89 to Thr-98, Ala-
	131 to Ser-142, Phe-169 to Cys-176, Gly-183 to Ser-193, Phe-202 to Pro-209, Arg-243
	to Ala-249, Ser-256 to Lys-265, Arg-277 to Asp-284.
838754	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1268 as
	residues: Phe-27 to Ser-37, Tyr-91 to Arg-96, Pro-156 to Gln-164, Cys-207 to Val-
	216, Met-242 to Tyr-251.
839561	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1271 as
	residues: Arg-2 to Gly-7, Arg-16 to Gln-22, Phe-41 to Gly-49, Ala-60 to Asn-74, Leu-
	125 to Gin-131, Asp-170 to Pro-175, Ala-209 to Arg-218, Glu-222 to Glu-258, Ala-265
020016	to Ser-300.
839816	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1272 as
940069	residues: His-32 to Arg-37, Ser-42 to Ser-48, Glu-77 to Glu-88.
840068	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1273 as residues: Ala-1 to Gln-14.
840279	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1274 as
040279	residues: Ala-1 to Asp-15.
840538	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1276 as
040550	residues: Ala-8 to Pro-13, Pro-18 to Gln-26, Lys-107 to Pro-114, Ala-149 to Arg-157,
	Ile-294 to Leu-299, Ser-356 to Pro-363, Pro-384 to Phe-392, Ala-474 to Gly-481, Ala-
	489 to Tyr-494, Pro-512 to Lys-517, Arg-623 to Thr-630, Lys-673 to Ser-678, Thr-703
	to His-709, Arg-714 to Arg-720, Gly-755 to Glu-766.
840549	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1278 as
	residues: Ala-5 to Lys-15, Pro-28 to Gln-34, Tyr-105 to His-111, Gln-150 to Cys-157.
840557	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1280 as
-	residues: Gly-34 to Leu-40, Thr-125 to Gly-134, Ala-148 to Arg-156, Lys-196 to Lys-
	215.
840561	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1281 as
<u> </u>	residues: Ser-21 to Phe-30.
840562	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1282 as
	residues: Gln-33 to Arg-41, Tyr-66 to Glu-71, Thr-112 to Gly-118, Thr-141 to Gly-
	148, Thr-160 to Cys-168, Arg-171 to Gly-177, Thr-180 to Pro-191, Glu-217 to Asp-
040564	225, Asp-236 to Lys-243.
840564	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1283 as
940400	residues: Val-13 to Pro-19, Gln-34 to Gly-39.
840600	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1285 as residues: Leu-26 to Ile-39.
840620	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1288 as
	residues: Ser-17 to Ser-26, His-32 to Gly-42, Thr-78 to Gln-83, Asp-130 to Leu-136,
	Arg-158 to Pro-164.
840626	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1290 as
	residues: Phe-7 to Tyr-13, Pro-19 to Ala-35, Asp-87 to Leu-96, Lys-98 to Glu-105,
040472	Glu-120 to Leu-133.
840638	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1291 as

	residues: Gly-8 to Leu-13, Gly-21 to Ser-31, Arg-45 to Arg-54.
840649	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1292 as
	residues: Asn-30 to Thr-37, Asp-44 to Lys-52, Ser-71 to Asp-80, Glu-127 to Glu-133,
	Arg-162 to Ala-173, Glu-191 to Leu-199.
840651	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1293 as
	residucs: Gly-14 to Glu-38, Asn-90 to Lys-100, Lys-150 to Val-158, Ser-166 to Gly-
	175.
840681	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1295 as
	residues: Thr-25 to Gly-31, Pro-86 to Trp-97, Ser-132 to Phe-138.
840682	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1296 as
	residues: Arg-12 to Lys-19, Asn-30 to Gly-36, Asp-50 to Gly-57, Glu-64 to Thr-69,
	Thr-79 to Lys-91, Gln-110 to Thr-115, Arg-223 to Gln-229, Asp-255 to Asp-260, Arg-
	278 to Gly-287, Glu-294 to Gln-300, Glu-433 to Glu-451, Leu-474 to Glu-479, Asp-
	490 to Leu-498, Gln-519 to Asp-527, Tyr-566 to Asp-575.
840684	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1297 as
	residues: Pro-1 to Ala-9, Val-56 to Val-63, Gly-86 to Glu-91.
840697	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1298 as
	residues: Pro-9 to Arg-15, Pro-36 to Ser-42, Ser-65 to Phe-72, Gly-99 to Ser-105, Ala-
	122 to Phe-129.
840698	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1299 as
	residues: Thr-75 to Pro-84, His-94 to Met-99, Asp-149 to Ile-168, Asn-370 to Asn-
<u></u>	375, Ser-384 to Lys-392, His-427 to Tyr-438.
840708	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1300 as
	residues: Ala-27 to Ser-36.
840714	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1301 as
1	residues: Gly-1 to Gly-20, Arg-54 to His-59, Asn-89 to Leu-95, Scr-119 to Lys-125, Trp-127 to Cys-133, Gln-175 to Gln-185, Asp-213 to Lys-222, Pro-267 to Gln-275,
	Asp-306 to Asp-313, Thr-321 to Cys-331.
840716	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1302 as
840/10	residues: Asn-40 to Thr-45, His-210 to Pro-215, Glu-369 to Thr-375, Lys-383 to Leu-
	397, Pro-438 to Ile-447, Pro-510 to Tyr-520, Arg-528 to Arg-533, Thr-549 to Thr-555.
840721	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1303 as
0,0,2,	residues: Arg-1 to Arg-7, Pro-29 to Lys-56, Asp-103 to Arg-108, Tyr-122 to Ser-127,
1	Gly-219 to Glu-227, Asp-250 to Glu-255, Glu-294 to Pro-301, Ala-321 to Tyr-327,
	Arg-367 to Pro-373, Glu-396 to Asn-405, Gly-411 to Arg-418, Asn-433 to Lys-441.
840735	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1304 as
	residues: Glu-1 to Gly-11, Thr-20 to Asp-40, Gly-51 to Glu-61, Ala-64 to Leu-78,
j .	Leu-82 to Arg-94.
840738	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1305 as
	residues: Gln-26 to Asn-34.
840745	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1306 as
ľ	residues: Gln-7 to Gly-12, Leu-60 to Pro-65, Arg-85 to Lys-99, Ser-132 to Pro-145,
	Pro-150 to Asp-155, Pro-183 to Asn-193, Arg-200 to Tyr-206.
840747	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1307 as
Ì	residues: Gln-1 to Asp-15, lle-35 to Glu-41, Leu-66 to Asn-71, Leu-73 to Pro-79, Gln-
	87 to Lys-94, Val-117 to Arg-123, Pro-144 to Tyr-150.
840756	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1308 as
	residues: Arg-8 to Gln-19, Arg-25 to Lys-38.
840776	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1309 as
	residues: Val-2 to Pro-10, Ser-28 to Ala-33, Pro-39 to Tyr-44, Thr-46 to Trp-55, Ser-
04070:	64 to Ser-72, Ala-103 to Pro-109, Pro-111 to Gln-118.
840784	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1310 as
1	residues: Pro-9 to Gly-20, Asn-32 to Leu-42, Asn-60 to Lys-70, Pro-76 to Gln-81, Glu-
040700	86 to Val-93, Arg-106 to Arg-111, Lys-176 to Asn-183. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1311 as
840788	residues: Ser-1 to Gln-8, Val-40 to Ser-49, Arg-105 to Lys-110.
L	residues. Ser-1 to Cin-8, Var-40 to Ser-47, Arg-103 to Eys-110.

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840794	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1312 as residues: Arg-1 to Gln-14. Arg-43 to Glu-54.
840797	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1313 as residues: Gly-1 to Arg-9, Asn-31 to Asp-37, Arg-44 to Asn-53, Gly-62 to Lys-77, Thr-123 to Ile-137, Gly-389 to Thr-394, Lys-486 to Asn-493, Glu-512 to Phe-520, Met-555 to Lys-560, Leu-618 to Ser-623, Ile-698 to Glu-706, Gly-723 to Leu-730, Ala-773 to Gln-790.
840818	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1315 as residues: Pro-1 to Ile-12. Asp-30 to Tyr-35, Leu-38 to Pro-45, Lys-54 to Thr-60, Thr-75 to Leu-80, Asp-92 to Tyr-100, Ile-133 to Thr-138, Thr-194 to Glu-199, Asp-233 to Leu-239, Met-243 to Ala-251, Asp-254 to Glu-261.
840822	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1316 as residues: Val-100 to Tyr-106, Ala-127 to His-135, Gln-153 to Lys-158, Gly-214 to Glu-219, Gln-236 to His-244, Lys-253 to Tyr-258.
840846	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1318 as residues: Ala-20 to Thr-27, Glu-47 to Tyr-57, Tyr-87 to Lys-95, Pro-121 to Ala-127, Pro-208 to Ala-224.
840848	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1319 as residues: Arg-77 to Asn-82, Glu-119 to Arg-124, Gln-156 to Thr-162, Lys-209 to Lys-215.
840860	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1320 as residues: Ile-27 to Asp-41, Glu-43 to Ala-58, Glu-149 to Glu-154, Lys-158 to Ile-165, Glu-167 to Gly-189, Glu-242 to Phe-247, Arg-259 to Phe-268, Ile-283 to Val-291, Thr-295 to Thr-307, Glu-328 to Asp-338, Asp-372 to Gly-387.
840871	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1322 as residues: Gly-31 to Tyr-38. Leu-40 to Leu-45, Pro-203 to Trp-208.
840874	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1323 as residues: Ala-23 to Gly-28.
840878	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1324 as residues: Thr-40 to Glu-46, Pro-69 to Arg-76, Glu-108 to Asp-150.
840880	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1325 as residues: Ser-5 to Lys-14, Phe-32 to Gln-37.
840884	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1326 as residues: Leu-4 to Ser-10.
840926	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1328 as residues: Met-6 to Thr-15, Ser-17 to Phe-37, Ser-148 to Lys-154, Lys-260 to Phe-276, Glu-285 to Ile-292, Lys-410 to Asp-424.
840932	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1329 as residues: Tyr-75 to Pro-83, Ile-181 to Gln-191, Glu-267 to Leu-275, Met-301 to Ala-307, Phe-322 to Gln-328, Met-371 to Gly-381, Gln-458 to Leu-463, Glu-474 to Lys-480, Lys-551 to Ser-558.
840940	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1330 as residues: Ser-26 to Thr-34, Thr-80 to Lys-88.
840947	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1331 as residues: Ile-1 to Arg-11, Pro-19 to Gln-46, Ala-55 to Pro-62, Cys-65 to Cys-82, Lys-93 to Pro-108.
840964	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1333 as residues: Ser-41 to Cys-46.
840979	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1334 as residues: Tyr-10 to His-27, Tyr-31 to Arg-41, Thr-44 to Leu-61, Cys-68 to Phe-73, Lys-98 to Glu-106, Gln-132 to Val-142, Glu-184 to Leu-191.
840984	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1335 as residues: Arg-38 to Gln-48, Met-137 to Asn-144, Gln-167 to Gln-172, Lys-182 to Gln-189, Gln-196 to Glu-206, Ile-210 to Glu-223, Gln-225 to Arg-246, Glu-250 to Thr-269, Gln-296 to Ile-318, Arg-323 to Glu-328, Tyr-337 to Lys-343, Glu-349 to Thr-357, Ser-393 to Glu-403, Arg-405 to Ile-427, Arg-431 to Glu-442, Leu-446 to Lys-473, Glu-475

ĺ	to Leu-486, Ile-488 to Asp-503, Ser-505 to Arg-623, Ala-625 to Asn-631, His-634 to
	Trp-792, Gly-799 to Gly-870, Arg-872 to Glu-929, Ser-931 to Pro-954, Ala-957 to Ala-
	977, Glu-982 to Trp-1000.
840986	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1336 as
1	residues: Asp-41 to Tyr-51.
840988	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1337 as
040700	residues: Pro-17 to Leu-31, Ser-95 to Val-100, Lys-123 to Gly-129.
040000	
840990	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1338 as
l	residues: Met-9 to Glu-16, Glu-41 to Trp-47, Arg-55 to Glu-62, Asp-135 to Ile-146,
	Gly-154 to Gly-160, Met-207 to Phe-214, Ser-245 to Lys-252, Gln-282 to Gln-288.
841009	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1340 as
	residues: Glu-12 to Thr-27, Met-45 to Asn-52, Tyr-79 to Thr-87, Asp-97 to Gly-102,
	Met-112 to Asp-120, Pro-141 to Tyr-155.
841012	Preferred epitopes include those comprising a sequence shown in SEQ 1D NO. 1341 as
	residues: Lys-36 to Ile-44, Arg-49 to Lys-69.
841016	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1342 as
•	residues: Cys-75 to His-82, Asp-126 to Tyr-135, Pro-144 to Tyr-155, Gly-179 to Trp-
	198, Tyr-201 to Met-208, Pro-226 to Lys-234, Gln-249 to Asp-267.
841017	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1343 as
041011	residues: Gln-1 to Trp-19.
841021	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1344 as
841021	1
041020	residues: Glu-58 to Gly-63, Leu-75 to Leu-82.
841032	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1345 as
	residues: Pro-1 to Gly-13, Pro-30 to Ser-57, Gln-61 to Thr-77, Arg-82 to Thr-88, Pro-
	100 to Lys-105, Gly-119 to Gly-126.
841051	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1346 as
	residues: Asn-1 to Lys-6, Thr-16 to Glu-21, Asn-45 to Ser-58, Asp-68 to Ser-75.
841064	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1347 as
	residues: Asp-53 to Pro-58, Glu-78 to Lys-85, Pro-95 to Arg-102, Ser-142 to Arg-148,
	Lys-209 to Arg-214, Lys-241 to Gly-246, Ser-287 to Leu-292, Lys-307 to Val-313,
	Arg-389 to Gln-394.
841069	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1348 as
	residues: Thr-1 to Trp-14, Lys-27 to Leu-44, Glu-59 to Arg-73, Lys-87 to Phe-95, Pro-
	160 to Asn-166, Leu-212 to Ile-220, Arg-236 to Asp-243.
841072	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1349 as
	residues: Pro-7 to Arg-12, Phe-71 to Gln-76, Arg-82 to Asp-98, Ala-108 to Glu-128.
841078	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1350 as
0070	residues: Arg-32 to Ala-39.
841080	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1351 as
041000	residues: Glu-1 to Gly-7, Glu-25 to Gly-33, Ala-54 to Phe-60, Gly-64 to Gln-108, Glu-
	116 to Ser-122, Pro-130 to Asn-138, Gln-141 to Lys-153, Arg-164 to Ser-172, Leu-186
	to Met-194, Pro-197 to Tyr-205, Asp-218 to Lys-229, Thr-236 to Ser-246, Ala-259 to
	Trp-266, Pro-281 to Pro-287, Cys-291 to Gln-298.
841092	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1353 as
	residues: Glu-45 to Lys-50.
841095	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1354 as
	residues: Lys-1 to Ser-19, Gly-33 to Gly-63, Gly-77 to Pro-89, Ser-164 to Ser-180,
	Ser-233 to Lys-238, Lys-267 to Leu-286.
841096	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1355 as
	residues: Gly-5 to Leu-12, Tyr-18 to Asp-25, Ile-88 to Ala-125, Ser-129 to Tyr-141,
	Gln-191 to Gln-196, Thr-290 to Asn-296, Thr-301 to Thr-309, Leu-360 to Ala-365,
	Leu-367 to Gly-378, Pro-398 to Gly-418, Pro-443 to Gly-454.
841102	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1356 as
071102	residues: Ser-61 to Leu-71.
9/11/0	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1358 as
841108	residues: Ala-8 to Leu-20, Lys-27 to Arg-33, Arg-40 to Ala-50, Asp-77 to Glu-84,

	Asn-99 to Gly-109.
841119	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1360 as
	residues: Lys-6 to Ala-14, Ile-68 to Asn-73, Val-84 to Leu-90, Glu-110 to Val-116,
	Leu-182 to Gly-190. Tyr-264 to Phe-270, Ile-300 to Lys-306, Pro-354 to Glu-367.
841124	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1361 as
211112	residues: Ser-21 to Thr-26.
841143	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1363 as
	residues: Thr-1 to Lys-9, Pro-20 to Gly-27, Gly-29 to Gly-52, Arg-54 to Gly-61, Gly-
-	69 to Gly-75, Ser-79 to Gly-96, Val-130 to Arg-135, His-207 to Asp-212, Val-296 to
841148	Leu-310, Arg-327 to Asn-334. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1364 as
041140	residues: Pro-1 to Met-43, Pro-55 to Ala-66, Pro-118 to Glu-128, Arg-181 to Lys-192,
	Tyr-197 to Thr-207, Trp-278 to Cys-284, Arg-334 to Asp-349.
841155	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1367 as
641133	residues: Gly-9 to Arg-24, Glu-69 to Met-74, Leu-86 to Leu-92, Asp-95 to Arg-115.
841163	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1370 as
041103	residues: Gly-29 to Gly-35, Ala-37 to Ala-48, Arg-97 to Thr-102, Arg-114 to Leu-119,
	Lys-144 to Lys-155.
841169	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1371 as
	residues: Ala-31 to Thr-69, Pro-90 to Pro-95, Pro-117 to Trp-126, Pro-128 to Arg-136.
841172	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1372 as
	residues: Gly-17 to Arg-35, His-76 to Pro-90, Pro-92 to Cys-103.
841174	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1373 as
	residues: Arg-1 to Arg-8, Arg-14 to Phe-19.
841179	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1374 as
	residues: Leu-4 to Met-10, Leu-17 to Tyr-36, Arg-38 to Asp-63, Tyr-82 to Glu-90,
l	Pro-97 to Gly-134, Arg-137 to Pro-148, Thr-160 to Lys-171, Tyr-183 to Asn-228, Gln-
	249 to Asn-258, Arg-263 to Glu-271, Arg-277 to Gln-296, Phe-298 to Asp-320, Glu-
	322 to Lys-329, Thr-337 to Thr-343, Glu-356 to Arg-363, Gly-371 to Asp-384.
841183	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1375 as
1	residues: His-1 to Ser-27, Arg-60 to Arg-73, Arg-96 to Asp-124, Asp-131 to Gly-143, Lys-145 to Glu-150.
841186	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1376 as
041100	residues: Leu-7 to Val-18, Ser-27 to Pro-57, Arg-124 to Thr-135, Pro-212 to Ser-230,
1	Gly-282 to Lys-287, Lys-441 to Lys-448.
841204	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1377 as
	residues: Lys-29 to Arg-35, Glu-81 to Arg-87, Ala-251 to Glu-261, Thr-266 to Gly-
	271, Thr-289 to Glu-295, Gly-328 to Tyr-334, Phe-432 to Lys-438, Asn-440 to Trp-
	458.
841206	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1378 as
	residues: Val-17 to Pro-25, Thr-55 to Asp-70, Lys-75 to Leu-81.
841207	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1379 as
	residues: Pro-9 to Glu-15, Arg-22 to Trp-32, Ser-54 to Glu-62, Asn-92 to Gly-103.
841211	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1380 as
	residues: Arg-7 to Gly-12, Met-42 to Ser-58, Gln-65 to Asn-73, Glu-91 to Ala-99, Pro-
041225	103 to Tyr-109, Arg-174 to Ala-179, His-189 to Gln-196, Asn-208 to Pro-219.
841225	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1381 as
841227	residues: Ala-32 to Ala-40, Glu-93 to Phe-103, Lys-173 to Thr-189. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1383 as
841237	residues: Arg-2 to Gln-12, Lys-76 to Ala-86, Tyr-155 to Lys-163, Glu-228 to Leu-234,
	Lys-263 to Lys-273. Ile-286 to Lys-296.
841241	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1384 as
071271	residues: Asp-41 to lle-52, Thr-59 to Lys-64, Glu-75 to Asn-89, Thr-99 to Thr-105.
841259	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1385 as
011437	residues: His-1 to Cys-22, Pro-24 to Pro-30, Tyr-84 to Ser-90, Ser-108 to Glu-118,
	Val-126 to Arg-143, Asp-175 to Gln-181, Ser-217 to Gly-224, Cys-262 to Cvs-270.
	

841260 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1386 as residues: Ala-25 to Glu-32, Ala-48 to Phe-53, Ser-69 to Ser-76, Asp-80 to Glu-86, Ser-125 to Ser-132, Ser-168 to Glu-179, Asn-201 to Ala-206, Lys-216 to Ile-246, Met-259 to Asn-272, Tyr-277 to Gln-287. 841264 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1387 as residues: Met-34 to Gly-50, Asp-69 to Trp-90, Asp-99 to Lys-107, Val-164 to Thr-170. 841311 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1389 as residues: Arg-4 to Val-15. 841313 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1390 as residues: His-6 to Gly-16, Gly-60 to Pro-95, Pro-125 to Gly-131, Gly-138 to Ala-147, Gln-173 to Glu-178. 841312 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1392 as residues: Lys-6 to Arg-23, Ser-74 to Arg-86, Lys-116 to Lys-122, Ser-127 to His-133, Ser-269 to Pro-275, Glu-344 to Phe-350, Gly-356 to His-362. 841331 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1393 as residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu-283. 841332 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1394 as residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Leu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-333 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1030 to Thr-709, Glu-191 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, T		Tue 206 to Clu 202 The 217 to The 224 Cle 241 to Cle 248 Tee 204 to Dec 200
residues: Met-34 to Gly-50, Asp-69 to Trp-90, Asp-99 to Lys-107, Val-164 to Thr-170. 841311 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1389 as residues: Arg4 to Val-15. 841313 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1390 as residues: His-6 to Gly-16, Gly-60 to Pro-95, Pro-125 to Gly-131, Gly-138 to Ala-147, Gln-173 to Glu-178. 841322 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1392 as residues: Lys-6 to Arg-23, Ser-74 to Arg-86, Lys-116 to Lys-122, Ser-127 to His-133, Ser-269 to Pro-275, Glu-344 to Phe-350, Gly-356 to His-362. 841331 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1393 as residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu-285. 841332 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1394 as residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Leu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-535 to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838 to Thr-850, Ser-832 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-121 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as residues: Ser-13 to Ser-18, Phe-48 to Ser-54. 841345 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-81 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-200, Val-224 to Glu-327, Thr-355 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-660, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-598	841260	residucs: Ala-25 to Glu-32, Ala-48 to Phe-53, Ser-69 to Ser-76, Asp-80 to Glu-86, Ser-125 to Ser-132, Ser-168 to Glu-179, Asn-201 to Ala-206, Lys-216 to Ile-246, Met-259
residues: Arg. 4 to Val-15. 841313 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1390 as residues: His-6 to Gly-16, Gly-60 to Pro-95, Pro-125 to Gly-131, Gly-138 to Ala-147, Gln-173 to Glu-178. 841322 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1392 as residues: Lys-6 to Arg-23, Ser-74 to Arg-86, Lys-116 to Lys-122, Ser-127 to His-133, Ser-269 to Pro-275, Glu-344 to Phe-350, Gly-356 to His-362. 841331 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1393 as residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu-285. 841332 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1394 as residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Leu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-353 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-353 to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838 to Thr-830, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-819 to Lys-835, Leu-867 to Asn-875, Leu-902 to Arg-910. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Asp-13 to Arg-18,		residues: Met-34 to Gly-50, Asp-69 to Trp-90, Asp-99 to Lys-107, Val-164 to Thr-170.
residues: His-6 to Gly-16, Gly-60 to Pro-95, Pro-125 to Gly-131, Gly-138 to Ala-147, Gln-173 to Glu-178. 841322 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1392 as residues: Lys-6 to Arg-23, Ser-74 to Arg-86, Lys-116 to Lys-122, Ser-127 to His-133, Ser-269 to Pro-275, Glu-344 to Phe-350, Gly-336 to His-362. 841331 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1393 as residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu-285. 841332 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1394 as residues: Glu-8 to Ser-13, Lys-20 to Glu-27A, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Leu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-335 to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838, En Thr-850, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as residues: Ser-13 to Ser-18, Phe-48 to Ser-54. 841345 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-819 to Lys-835, Leu-867 to Asn-875, Leu-902 to Arg-910. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Arg-18, Pro-36 to Arg-43, Gly-66 to Ser-74, Gly-87 to Lys-92, Asp-11	841311	
residues: Lys-6 to Arg-23, Ser-74 to Arg-86, Lys-116 to Lys-122, Ser-127 to His-133, Ser-269 to Pro-275, Glu-344 to Phe-350, Gly-356 to His-362. 841331 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1393 as residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu-285. 841332 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1394 as residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Lcu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-351s to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838 to Thr-850, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as residues: Ser-13 to Ser-18, Phe-48 to Ser-54. 841345 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Arg-446 to Glu-525, Gln-55 to Lys-69. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Asn-13 to Arg-18, Pro-36 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. 84	841313	residues: His-6 to Gly-16, Gly-60 to Pro-95, Pro-125 to Gly-131, Gly-138 to Ala-147,
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1393 as residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu-285. 841332 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1394 as residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Lcu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-535 to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838 to Thr-850, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Ily-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as residues: Ser-13 to Ser-18, Phe-48 to Ser-54. 841345 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-220, Val-224 to Glu-322, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-220, Val-224 to Glu-322, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-220, Val-224 to Glu-322, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-220, Val-224 to Glu-322, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-220, Val-224 to Glu-321, Leu-902 to Arg-910. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1397 as residues: Arg-13 to Glu-415, Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Ser-73. 841817 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Trr-1 to Ser-20. 841835 Preferred epitopes include those comp	841322	residues: Lys-6 to Arg-23, Ser-74 to Arg-86, Lys-116 to Lys-122, Ser-127 to His-133,
residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Leu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-535 to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838 to Thr-850, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-1217, Pro-1277 to Leu-1282. 841338 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as residues: Ser-13 to Ser-18, Phe-48 to Ser-54. 841345 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-819 to Lys-835, Leu-867 to Asn-875, Leu-902 to Arg-910. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1397 as residues: Asp-13 to Arg-18, Pro-36 to Arg-43, Gly-66 to Ser-74, Gly-87 to Lys-92, Asp-110 to Glu-115. 841417 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Lys-69. 841632 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Trr-1 to Ser-20. 841837 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Trr-1 to Ser-20. 841839 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-216 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. 842259 Preferred epitopes include those comprising	841331	residues: Ser-45 to Lys-67, Asp-155 to Asp-172, Gln-193 to Ile-199, Gln-271 to Glu- 285.
841348 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as residues: Ser-13 to Ser-18, Phe-48 to Ser-54. 841345 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-819 to Lys-835, Leu-867 to Asn-875, Leu-902 to Arg-910. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1397 as residues: Asp-13 to Arg-18, Pro-36 to Arg-43, Gly-66 to Ser-74, Gly-87 to Lys-92, Asp-110 to Glu-115. 841417 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1399 as residues: Leu-102 to Ile-111, Pro-131 to Ile-337, Thr-339 to Asp-376. 841632 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Lys-69. 841771 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Pro-22 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. 841827 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Thr-1 to Ser-20. 841835 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. 842259 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. 842463 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Cys-74 to Tyr-79. 842595 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79.	841332	residues: Glu-8 to Ser-13, Lys-20 to Glu-27, Arg-81 to Ser-94, Thr-147 to Ile-154, Asn-200 to Glu-212, Asn-235 to Gly-244, Leu-433 to Thr-439, Pro-444 to Asn-455, Ser-470 to Asp-476, Ser-492 to Met-499, Glu-535 to Pro-547, Glu-703 to Thr-709, Glu-719 to Thr-726, Asn-802 to Leu-807, Asn-820 to Arg-825, Lys-830 to Tyr-836, Thr-838 to Thr-850, Ser-882 to Ser-894, Lys-944 to Gly-952, Gly-969 to Val-977, Glu-984 to Asn-990, Arg-996 to Lys-1001, Pro-1032 to Leu-1039, Thr-1050 to Gly-1058, Val-1103 to Arg-1108, Pro-1160 to His-1169, Tyr-1180 to Ser-1187, Glu-1211 to Ser-
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1396 as residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu-220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu-327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-819 to Lys-835, Leu-867 to Asn-875, Leu-902 to Arg-910. 841349 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1397 as residues: Asp-13 to Arg-18, Pro-36 to Arg-43, Gly-66 to Ser-74, Gly-87 to Lys-92, Asp-110 to Glu-115. 841417 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1399 as residues: Leu-102 to Ile-111, Pro-131 to Ile-337, Thr-339 to Asp-376. 841632 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Lys-69. 841771 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Pro-22 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. 841827 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. 842259 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. 842463 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. 84259 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79.	841338	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1395 as
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1397 as residues: Asp-13 to Arg-18, Pro-36 to Arg-43, Gly-66 to Ser-74, Gly-87 to Lys-92, Asp-110 to Glu-115. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1399 as residues: Leu-102 to Ile-111, Pro-131 to Ile-337, Thr-339 to Asp-376. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Lys-69. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Pro-22 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Thr-1 to Ser-20. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841345	residues: Trp-83 to Thr-89, Ser-135 to Asn-140, Ser-185 to Cys-190, Tyr-209 to Glu- 220, Val-224 to Glu-232, Leu-258 to Asn-263, Ser-306 to Asn-312, Thr-319 to Glu- 327, Thr-365 to Ile-373, Gly-417 to Cys-429, Lys-439 to Val-445, Lys-464 to Leu-469, Leu-477 to Asn-485, Arg-546 to Val-554, Glu-598 to Gly-607, Pro-634 to Ser-639, Asn-730 to Ala-746, Lys-812 to Gln-817, Glu-819 to Lys-835, Leu-867 to Asn-875,
residues: Leu-102 to Ile-111, Pro-131 to Ile-337, Thr-339 to Asp-376. 841632 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Lys-69. 841771 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Pro-22 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. 841827 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Thr-1 to Ser-20. 841835 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. 842259 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. 842463 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. 842595 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841349	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1397 as residues: Asp-13 to Arg-18, Pro-36 to Arg-43, Gly-66 to Ser-74, Gly-87 to Lys-92,
residues: Arg-13 to Gly-40, Arg-46 to Glu-52, Gln-55 to Lys-69. 841771 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Pro-22 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. 841827 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Thr-1 to Ser-20. 841835 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. 842259 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. 842463 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. 842595 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841417	
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as residues: Pro-22 to Gly-30, Asp-45 to Gln-56, Ser-67 to Ser-73. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Thr-1 to Ser-20. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841632	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1401 as
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as residues: Thr-1 to Ser-20. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841771	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1403 as
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as residues: Tyr-5 to Lys-13, Cys-52 to Arg-61, Cys-85 to Ala-91, Gly-122 to Asn-127. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841827	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1404 as
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as residues: Pro-16 to Gly-23, Glu-37 to Pro-45, Gly-52 to Ser-57. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	841835	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1405 as
Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	842259	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1406 as
842595 Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as	842463	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1407 as residues: Cys-74 to Tyr-79.
	842595	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1408 as

<u></u>	226, Glu-257 to Lys-271. Gln-280 to Leu-289.
842722	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1409 as
]	residues: Glu-9 to Arg-20. Ser-48 to Lys-56, Ile-69 to Glu-81. Pro-83 to Lys-89, Lys-
l	94 to Ile-99, Pro-104 to Gly-110, Glu-116 to Asp-133, Ile-140 to Ser-154, Gln-206 to
	His-217, Pro-219 to Leu-231. Arg-237 to Lys-243. Gln-247 to Pro-256, Leu-271 to
	Thr-283, Lys-289 to Lys-294. Ser-338 to Lys-355, Gly-375 to Thr-381, Scr-428 to Pro-
	454. Gly-460 to Gln-467. Lys-480 to Lys-488.
842818	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1411 as
	residues: Ala-25 to Ala-30. Lys-32 to Ala-51, Gln-61 to Ala-68, Glu-83 to Lys-91,
	Phe-99 to Glu-105, Glu-123 to Gly-129.
843251	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1412 as
	residues: Pro-30 to Ser-40, Lys-47 to Thr-52, Val-59 to Pro-64, Lys-129 to Arg-134.
	Leu-169 to Asp-177.
843422	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1413 as
	residues: Thr-9 to Lys-20, Lys-25 to Cys-31, Pro-33 to Tyr-42, Asn-76 to Lys-84, Leu-
	102 to Trp-112.
843784	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1414 as
	residues: Leu-16 to Thr-24, Glu-41 to Gln-47, Lys-64 to Cys-72, Thr-87 to Ser-100,
	Pro-130 to Asn-143, Thr-163 to Asp-170.
844017	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1415 as
	residues: Leu-11 to Ile-17, Leu-30 to Met-45.
844138	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1416 as
	residues: Lys-19 to Thr-28, Arg-47 to Gln-52, Leu-73 to Leu-81, Asp-122 to Phe-131,
	Ala-135 to Ser-148, Pro-155 to Asp-163, Ser-184 to His-191, Leu-219 to Asn-225,
	Asp-238 to Thr-248, Pro-253 to Cys-259, Cys-356 to His-368, Ser-426 to Gly-435,
	Pro-467 to Cys-478, Glu-504 to Cys-509, His-553 to Gly-568, Ala-581 to Cys-586,
	Ala-595 to Cys-600, Arg-602 to Trp-608.
844194	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1418 as
044704	residues: Pro-23 to Arg-31, Gln-79 to Gln-85, Cys-93 to Cys-107, Pro-216 to Leu-222.
844394	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1419 as
944460	residues: Arg-1 to Phe-11.
844450	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1420 as
	residues: Ser-37 to Trp-43, Pro-47 to Thr-55, Arg-60 to Lys-69, Tyr-125 to His-131,
844535	Pro-187 to Lys-195, Gly-346 to Lys-351. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1422 as
844333	residues: Asp-8 to Ala-18, Ser-47 to Ala-52, Thr-62 to Arg-69, Pro-119 to Asp-126,
:	Trp-164 to Thr-170, Ala-206 to Ala-213, Pro-230 to Gly-235, Lys-304 to Lys-314, Lys-341 to Val-347, Tyr-387 to Thr-398.
844644	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1423 as
UT1017	residues: Ala-9 to Asp-16, Asn-78 to Tyr-86.
844653	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1424 as
0.1000	residues: Arg-1 to Gly-8, Ala-30 to Gln-36.
844796	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1426 as
V	residues: His-12 to His-22.
844812	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1427 as
011012	residues: Gly-281 to Arg-290, Ala-349 to Ser-355, Glu-378 to Asp-388.
844894	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1428 as
2.1374	residues: Pro-2 to Phe-8, Ser-13 to Ala-34, Pro-37 to Phe-43, Lys-63 to Gly-73, Cys-
	88 to Asp-93, Gly-98 to Trp-103, Cys-273 to Ile-287, Ile-290 to Ser-296.
845361	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1429 as
	residues: Met-10 to Ile-21, Glu-108 to Lys-122, Lys-272 to Gly-280, Gly-298 to Lys-
	304. Trp-364 to Lys-369.
845620	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1430 as
	residues: Thr-62 to Ala-67, Leu-96 to Glu-101, Cys-184 to Trp-190.
845639	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1431 as
	residues: Arg-41 to Arg-48, Met-72 to Val-79, Gln-81 to Trp-89, Ala-96 to Asp-101,
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	Arg-110 to Gly-118, Asn-126 to Arg-135, Ala-144 to Asp-149, Leu-199 to Lys-213. Gln-245 to Glu-256, Arg-261 to Thr-267.
845660	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1432 as
ļ.	residues: Gly-5 to Leu-17, Arg-19 to Arg-29, Pro-36 to Arg-50, Arg-60 to Pro-67, Gln-
1	133 to Leu-150, Gln-168 to Phe-187, Pro-189 to Gln-194, Asp-240 to Gly-251, Thr-
1	308 to Cys-317, Val-325 to Glu-331. Leu-354 to Pro-369, Lys-381 to Cys-388, Arg-
1	410 to Phe-417.
845720	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1433 as
	residues: Thr-1 to Glu-11, Arg-21 to Pro-27, Pro-44 to His-49, Glu-56 to Leu-69, Ala-
	74 to Gly-80, Phc-82 to Pro-87.
845897	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1435 as
] .	residues: Gly-1 to Ser-9, Gly-31 to Ser-38, Arg-52 to Val-68, Leu-71 to Glu-84.
845922	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1436 as
ļ	residues: Asn-1 to Pro-6, Pro-29 to Gln-36, Glu-95 to Arg-100, Pro-150 to Met-157,
	Ser-272 to Tyr-278, Gly-289 to Arg-294, Lys-397 to Ser-403.
846040	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1438 as
	residues: Cys-6 to Ser-16, Glu-52 to Tyr-58, Asn-144 to Lys-153.
846073	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1439 as
	residues: Arg-6 to Thr-16, Ile-43 to Gln-48, Leu-131 to Gly-139, Gly-147 to Asp-155,
	Asp-191 to Asp-198, Gly-204 to Thr-214.
846257	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1440 as
	residues: Lys-24 to Phe-44, Arg-58 to Gly-64, Ser-69 to Val-75, Lys-83 to Leu-90,
	Lys-93 to Glu-106.
HTXPN06R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1441 as
	residues: Gly-1 to His-8.
HWAFU16R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1443 as
	residues: Ile-29 to Lys-34.
HOEMT44R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1445 as
	residues: Asp-73 to Lys-79.
HE2OW04R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1446 as
	residues: Cys-1 to Asn-6, Met-41 to Thr-51, Lys-77 to Thr-82.
HFCFG25R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1447 as
	residues: Lys-29 to Ile-37, Arg-42 to Lys-47.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1448 as
	residues: Pro-18 to Arg-23, Ala-43 to Ser-48.
H2CBI37R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1449 as
	residues: Gly-5 to Lys-19, Phe-26 to Trp-31.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1451 as
	residues: Leu-2 to Asn-8.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1453 as
	residues: Pro-20 to His-36.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1454 as
	residues: Tyr-15 to Ala-22, Ser-68 to Gly-74.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1456 as
	residues: Gly-1 to Tyr-6, Asp-40 to Thr-47, Lys-91 to Glu-97.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1458 as
	residues: Gly-31 to Gly-39.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1459 as
	residues: Asp-73 to Gly-78.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1461 as
	residues: Asn-19 to Gln-25, Arg-33 to Ala-42, Pro-92 to Lys-99.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1463 as
	residues: Lys-6 to Phe-13, His-25 to Ser-30, Glu-35 to Ala-41, Pro-57 to Gly-62.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1465 as
	residues: Leu-1 to Gly-6, Pro-29 to Gly-42, Lys-52 to Gly-62.
HOFOA89R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1467 as

	residues: Ala-20 to Lys-29, Arg-48 to Ile-56.
HCROL58R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1470 as
	residues: Lys-1 to Ser-16.
HCHMV24R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1473 as
	residues: Gly-4 to Lys-10, Gln-36 to Glu-41.
HCHPT49R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1474 as
	residues: Gly-4 to Lys-10, Gln-36 to Glu-41, Arg-61 to Arg-70.
HCHPESOR	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1477 as
111031113311	residues: Arg-10 to Lys-22.
HS2IA81R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1478 as
HISZIMOTK	residues: Gly-4 to Lys-10, Gln-36 to Glu-41, Arg-61 to Arg-76.
HCPNC17P	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1479 as
I CKINCI /K	residues: Gly-4 to Lys-10, Gln-36 to Glu-41, Arg-61 to Arg-76, Lys-107 to Pro-112.
HISDIZOR	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1480 as
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HASCCZIR	residues: Gly-4 to Lys-10, Gln-36 to Glu-41, Arg-61 to Arg-76.
HASCG/IK	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1482 as
1105140420	residues: Lys-6 to Ile-13.
HOEMO43R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1483 as
140145 015	residues: Lys-31 to Gln-43.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1486 as
	residues: Pro-1 to Glu-7, Asp-42 to Gly-47, Leu-61 to Glu-69, Lys-97 to Ile-107, Asp-
	115 to Gly-120.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1490 as
	residues: Ala-18 to Asp-26.
HLQFY41R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1491 as
	residues: Val-11 to Asp-16, Glu-46 to Arg-51, Pro-55 to Lys-61, Lys-82 to Val-87.
HOFMO83R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1492 as
	residues: Thr-31 to Asp-39, Thr-52 to Gly-60.
HFTDR22R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1493 as
	residues: Glu-1 to Trp-13.
HOEKC39R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1495 as
[residues: Tyr-25 to Phe-32.
HOSNR06R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1498 as
	residues: Thr-1 to Tyr-7.
HCQDL20R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1499 as
	residues: Ser-12 to His-21.
HFKHD49R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1503 as
	residues: Ala-42 to Glu-68.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1506 as
	residues: Ala-1 to Leu-9.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1507 as
	residues: Lys-7 to Thr-13, Asp-24 to Thr-30, Gly-39 to Glu-52, Leu-70 to Ile-78.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1510 as
	residues: Thr-2 to Asn-12, Gly-14 to Arg-24.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1512 as
	residues: Pro-1 to Glu-8, Ala-10 to Gly-26.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1513 as
	residues: Glu-53 to Ser-59, His-121 to Gln-130.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1515 as
	residues: Gly-49 to Glu-64, Phe-76 to Thr-81.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1518 as
	residues: Arg-1 to Gln-26, Phe-59 to Lys-68.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1519 as
	residues: Asp-1 to Lys-8, Asp-35 to Glu-41.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1520 as
	residues: Cys-1 to Leu-15.

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HABGF46R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1527 as residues: Arg-11 to Arg-20, Asn-42 to Pro-57, Arg-64 to Ser-81.
HOELCISR	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1528 as residues: His-8 to Gly-18, Gln-56 to Arg-61.
H2LAR26R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1529 as residues: Glu-11 to Asn-16, Lys-38 to Glu-43, Ala-62 to Asp-67, Asp-80 to Ser-101.
H2LAV85R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1530 as residues: Pro-14 to Thr-25, Asp-89 to Gln-102, Ile-121 to Thr-131.
HBSDC92R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1531 as residues: Arg-1 to Leu-11.
HUTHN01R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1532 as residues: Pro-34 to Ser-42, Cys-82 to Lys-89.
H2LAW03R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1533 as residues: Arg-120 to Arg-127.
HOEMO60R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1534 as residues: Pro-6 to Arg-11, Phe-18 to Asn-23, Leu-36 to Thr-41.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1537 as residues: Arg-1 to Pro-14, Gln-47 to Cys-52.
HAPNX59R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1538 as residues: Cys-19 to Ser-25, Asp-28 to Trp-34, Lys-71 to Trp-76, Glu-112 to Lys-120.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1539 as residues: His-14 to Glu-26.
H2CBN02R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1542 as residues: Ala-1 to Pro-9, Arg-20 to Val-25.
H2CBV68R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1543 as residues: Pro-41 to Asp-46, Leu-56 to Lys-61, Ala-72 to Thr-83, Lys-100 to Asn-106, Leu-125 to Thr-133.
H6EDK07R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1544 as residues: Glu-32 to Glu-40, Val-45 to Thr-51, Pro-61 to Arg-67.
H2CBN54R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1547 as residues: Cys-36 to Tyr-44, Glu-55 to Asp-61, Arg-79 to Pro-84, Asp-89 to Pro-105, Cys-108 to Ala-118, Lys-126 to Gly-142.
HWHPX50R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1549 as residues: Pro-35 to Tyr-41.
HAPQD84R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1550 as residues: Lys-32 to Glu-39.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1554 as residues: Arg-46 to Arg-60, Glu-69 to Gly-78.
HODEV64R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1555 as residues: Glu-1 to Gly-27, Asn-34 to Phe-48, Gly-63 to Gly-68.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1558 as residues: Asp-27 to Gly-34, Ser-41 to Glu-49, Val-55 to Gln-62.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1559 as residues: Ile-17 to His-22, Ser-24 to Arg-29.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1560 as residues: Ser-10 to Asp-20, Leu-22 to Pro-36, Ser-42 to Lys-57, Gln-102 to Glu-110.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1561 as residues: Arg-1 to Glu-6, Asp-74 to Ser-79, Asp-122 to Thr-127.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1563 as residues: Arg-25 to His-31, Ala-50 to Ala-55.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1566 as residues: Val-56 to Cys-61, Thr-108 to Gln-122, Gln-125 to Lys-131, Glu-140 to Leu-146.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1567 as residues: Leu-3 to Ala-10, Pro-12 to Gly-21, Pro-32 to Pro-38, Ala-58 to Lys-64, Lys-67 to Val-75, Asp-92 to Leu-103.

HCLBZ27R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1570 as residues: Asp-12 to Glu-18, Ala-22 to Ilc-28, Ala-48 to Gly-60.
H2LAVIIR	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1571 as
	residues: Thr-5 to Thr-14, Arg-20 to His-25, Arg-35 to Gly-40, Lys-58 to Arg-66, His-
	101 to Ser-107, Arg-111 to Lys-125.
HOEMJ56R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1573 as
	residues: Lys-27 to Tyr-48.
HDPLP40R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1576 as
	residues: Gly-1 to Cys-24, Cys-27 to Gly-43, Ala-46 to Trp-54, Ala-56 to Arg-68, Phe-
	83 to Arg-93.
HABAD57R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1578 as
	residues: Gly-3 to Gln-16, Pro-36 to Ala-41.
H2CBL68R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1581 as
	residues: Pro-19 to Val-24. Thr-31 to Gln-38, His-103 to Lys-114, Arg-129 to Leu-
	137. Pro-139 to Ser-146.
HNTNE17R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1582 as
	residues: Val-8 to Lys-15, Tyr-25 to Asn-35, Lys-48 to Lys-53, Lcu-77 to Asn-87,
L	Asp-103 to Glu-108.
HBJLR37R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1583 as
	residues: Asn-1 to His-11, Pro-82 to Glu-89, Pro-91 to Asp-96, Arg-103 to Met-109.
HOSNG20R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1584 as
	residues: Thr-50 to Lys-55.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1586 as
	residues: Thr-10 to Trp-15, Leu-24 to Ala-30, Leu-32 to Glu-38, Asn-41 to Ala-59,
	Arg-81 to Asp-89, Lys-104 to Lys-111.
HOEKC80R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1587 as
	residues: Pro-49 to Phe-55, Gly-82 to Gly-88.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1589 as
	residues: Thr-12 to Leu-18.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1592 as
	residues: Glu-2 to Ile-9, Glu-34 to Lys-42.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1594 as
	residues: Gly-4 to Thr-13.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1595 as
	residues: Thr-2 to Asn-10, Glu-22 to Gln-30, Ser-58 to Gln-80, Gln-88 to Phe-96, Thr-
	99 to Tyr-104, Lys-110 to Asp-115. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1596 as
	residues: Trp-18 to Ser-26, Asp-91 to Trp-99.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1603 as
	residues: Ser-17 to Cys-25.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1609 as
	residues: Arg-1 to Lys-10, Ser-15 to Tyr-22, Gly-25 to Leu-31.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1615 as
	residues: Thr-38 to Trp-45, Pro-63 to Gln-70, Pro-78 to Gln-85.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1619 as
	residues: Pro-43 to Trp-50.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1621 as
	residues: Pro-17 to Pro-27, Pro-32 to Tyr-38, Ala-44 to Pro-49.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1627 as
	residues: Gln-3 to His-13, Gly-48 to Gly-55.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1628 as
	residues: Ser-16 to His-21, Ala-29 to Thr-35.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1629 as
	residues: Lys-20 to Lys-28, Ser-53 to Leu-60.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1630 as
	residues: Leu-1 to Leu-18.

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	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1633 as
	residues: Glu-I to Arg-28.
HCUDCSIR	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1634 as
	residues: Pro-22 to Gly-32. Trp-67 to Lys-81.
HDPFI40R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1635 as
	residues: Tyr-1 to Phe-6, Pro-9 to Asn-22, Arg-30 to Ala-38, Pro-47 to Lys-69.
HDPRZ54R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1637 as
	residues: Gly-1 to Ala-8.
HFAUO64R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1640 as
1	residues: Asn-7 to Lys-29.
HJMAU64R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1645 as
	residues: Leu-58 to Tyr-69.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1647 as
·	residues: Ser-16 to His-46, Arg-49 to Thr-58.
HKBAD57R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1648 as
	residues: Thr-23 to Ser-30.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1653 as
	residues: Pro-15 to Thr-20.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1655 as
	residues: Ala-7 to Ser-12.
HOEMO62R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1656 as
	residues: Ile-3 to Lys-11.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1658 as
	residues: Lys-37 to Asn-44.
HOGAP33R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1659 as
	residues: Gln-29 to Asp-35, Gln-43 to Thr-49.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1661 as
1	residues: Pro-29 to Arg-36.
HPIAC23R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1663 as
	residues: Thr-62 to Thr-69.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1664 as
	residues: Val-1 to Thr-6, Arg-64 to Arg-69.
HRADI57R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1666 as
	residues: Val-11 to Gln-16.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1667 as
ł	residues: Gly-7 to Thr-20.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1670 as
	residues: Ala-5 to Lys-11, Arg-29 to Ser-36.
HUTHF75R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1673 as
	residues: Lys-40 to Gly-47.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1674 as
R	residues: Phe-44 to Arg-49.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1676 as
	residues: Gly-29 to Asp-34.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1678 as
	residues: Lys-24 to Arg-29, Cys-34 to Ala-41.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1679 as
	residues: Leu-21 to Asp-38.
НАМНН32	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1680 as
	residues: Ala-1 to Cys-10, Glu-15 to Gln-21.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1683 as
	residues: Lys-17 to Thr-23.
	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 1684 as
	residues: Ser-3 to Lys-8, Trp-92 to Leu-97.
L	residues. Sei-3 to Lys-6, 11p-72 to Leu-27.

The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of the polypeptide sequence shown in SEQ ID NO:Y, or an epitope of the polypeptide sequence encoded by the cDNA in the related cDNA clone contained in a deposited library or encoded by a polynucleotide that hybridizes to the complement of an epitope encoding sequence of SEQ ID NO:X, or an epitope encoding sequence contained in the deposited cDNA clone under stringent hybridization conditions, or alternatively, under lower stringency hybridization conditions, as defined supra. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to this complementary strand under stringent hybridization conditions or alternatively, under lower stringency hybridization conditions, as defined supra.

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The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described infra. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross- reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

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In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe 20 et al., supra; Wilson et al., supra; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, in vivo immunization, in vitro immunization, and phage display methods. See, e.g., Sutcliffe et al., supra, Wilson et al., supra, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If in vivo immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

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As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention, and immunogenic and/or antigenic epitope fragments thereof can be fused to other polypeptide sequences. For example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof) resulting in chimeric polypeptides. Such fusion proteins may facilitate purification and may increase half-life in vivo. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light

chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., Nature, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion desulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., J. Biochem., 270:3958-3964 (1995).

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Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, may be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope

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derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

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Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin ("HA") tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., Proc. Natl. Acad. Sci. USA 88:8972-897 (1991)). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni2+ nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the

polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

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As discussed herein, any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

In certain preferred embodiments, proteins of the invention comprise fusion proteins wherein the polypeptides are N and/or C- terminal deletion mutants. In preferred embodiments, the application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to the nucleic acid sequences encoding polypeptides having the amino acid sequence of the specific N- and C-terminal deletions mutants. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell

or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

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Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples

of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells (e.g., Saccharomyces cerevisiae or Pichia pastoris (ATCC Accession No. 201178)); insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

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Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most

preferably, high performance liquid chromatography ("HPLC") is employed for purification.

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Polypeptides of the present invention can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

In one embodiment, the yeast *Pichia pastoris* is used to express polypeptides of the invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A main step in the methanol metabolization pathway is the oxidation of methanol to formaldehyde using O₂. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O₂. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOXI*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOXI* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. See, Ellis, S.B., et al., Mol. Cell. Biol. 5:1111-21 (1985); Koutz, P.J, et al., Yeast

5:167-77 (1989); Tschopp, J.F., et al., Nucl. Acids Res. 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the AOX1 regulatory sequence is expressed at exceptionally high levels in Pichia yeast grown in the presence of methanol.

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In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and

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which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

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In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., Nature, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4diaminobutyric acid, a-amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as bmethyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

Non-naturally occurring variants may be produced using art-known mutagenesis techniques, which include, but are not limited to oligonucleotide mediated mutagenesis, alanine scanning, PCR mutagenesis, site directed mutagenesis (see, e.g., Carter et al., Nucl. Acids Res. 13:4331 (1986); and Zoller et al., Nucl. Acids Res. 10:6487 (1982)), cassette mutagenesis (see, e.g., Wells et al., Gene 34:315

(1985)), restriction selection mutagenesis (see, e.g., Wells et al., Philos. Trans. R. Soc. London SerA 317:415 (1986)).

The invention additionally, encompasses polypeptides of the present invention which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

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Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between

about I kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the polyethylene glycol may have an average molecular weight of about 200; 500; 1000; 1500; 2000; 2500; 3000; 3500; 4000; 4500; 5000; 5500; 6000; 6500; 7000; 7500; 8000; 8500; 9000; 9500; 10,000; 10,500; 11,000; 11,500; 12,000; 12,500; 13,000; 13,500; 14,000; 14,500; 15,000; 15,500; 16,000; 16,500; 17,000; 17,500; 18,000; 18,500; 19,000; 19,500; 20,000; 25,000; 30,000; 35,000; 40,000; 50,000; 55,000; 60,000; 65,000; 70,000; 75,000; 80,000; 85,000; 90,000; 95,000; or 100,000 kDa.

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As noted above, the polyethylene glycol may have a branched structure. Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo et al., Appl. Biochem. Biotechnol. 56:59-72 (1996); Vorobjev et al., Nucleosides Nucleotides 18:2745-2750 (1999); and Caliceti et al., Bioconjug. Chem. 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, e.g., EP 0 401 384, herein incorporated by reference (coupling PEG to G-CSF), see also Malik et al., Exp. Hematol. 20:1028-1035 (1992) (reporting pegylation of GM-CSF using tresyl chloride). For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as, a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid

residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

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As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to a proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may 15 select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either directly or by an intervening linker. Linkerless systems for attaching polyethylene glycol to proteins are described in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992); Francis et al., Intern. J. of Hematol. 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.

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One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride (CISO₂CH₂CF₃). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoreothane sulphonyl group.

Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

The number of polyethylene glycol moieties attached to each protein of the invention (i.e., the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of

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substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992).

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The cancer antigen polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

Multimers encompassed by the invention may be homomers or heteromers. As used herein, the term homomer, refers to a multimer containing only polypeptides corresponding to the amino acid sequence of SEQ ID NO:Y or an amino acid sequence encoded by SEQ ID NO:X, and/or an amino acid sequence encoded by the cDNA in a related cDNA clone contained in a deposited library (including fragments, variants, splice variants, and fusion proteins, corresponding to any one of these as described herein). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (e.g., containing polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

As used herein, the term heteromer refers to a multimer containing one or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to

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the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

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Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked, by for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acidresidues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, or contained in a polypeptide encoded by SEQ ID NO:X, and/or by the cDNA in the related cDNA clone contained in a deposited library). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for

example, oseteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

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Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention

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containing Flag® polypeptide seuqence. In a further embodiment, associations proteins of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

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The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide components desired to be contained in the multimer of the invention (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a linker polypeptide and then further to a synthetic

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polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hyrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

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Antibodies

Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of SEQ ID NO:Y, and/or an epitope, of the present invention (as determined by immunoassays well known in the art for assaying specific antibodyantigen binding). Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule.

Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody

fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

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The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog,

or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or Kd less than 5 X 10⁻² M, 10^{-2} M, 5 X 10^{-3} M, 10^{-3} M, 5 X 10^{-4} M, 10^{-4} M, 5 X 10^{-5} M, 10^{-5} M, 5 X 10^{-6} M, 10^{-6} M, 5 X 10^{-7} M, 10^{7} M, 5 X 10^{-8} M, 10^{-8} M, 5 X 10^{-9} M, 10^{-9} M, 5 X 10^{-10} M, 10^{-10} M, 5 X 10^{-11} M, 10^{-11} M, 5 X 10^{-12} M, $^{10-12}$ M, 5 X 10^{-13} M, 10^{-13} M, 5 X 10^{-14} M, 10^{-13} M, 10^{-14} 14 M, 5 X 10^{-15} M, or $^{10-15}$ M.

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The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 50%.

Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferrably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described supra). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res.

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58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

Antibodies of the present invention may be used, for example, but not limited to, to purify, detect, and target the polypeptides of the present invention, including both in vitro and in vivo diagnostic and therapeutic methods. For example, the antibodies have use in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988) (incorporated by reference herein in its entirety).

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As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalently and non-covalently conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387.

The antibodies of the invention include derivatives that are modified, i.e, by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphylation, amidation, derivatization by known protecting/blocking groups,

proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

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The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of- interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: Monoclonal Antibodies and T-Cell Hybridomas 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

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Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')2 fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). F(ab')2 fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

For example, the antibodies of the present invention can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire

or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab. Fy or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

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As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')2 fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999

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(1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the nonhuman species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

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Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody

libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

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Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered nonfunctional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825;

5,661,016: 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix. Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., Bio/technology 12:899-903 (1988)).

Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand. For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligands/receptors, and thereby block its biological activity.

Polynucleotides Encoding Antibodies

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The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined supra, to polynucleotides that encode an antibody, preferably, that specifically binds to a

polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y.

The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., BioTechniques 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

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Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, Current Protocols in Molecular Biology, John Wiley &

Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

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In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well know in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a nonhuman antibody, as described supra. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed supra, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described supra, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived

from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423- 42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in E. coli may also be used (Skerra et al., Science 242:1038-1041 (1988)).

Methods of Producing Antibodies

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The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The invention, thus, provides replicable vectors comprising a

nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO,

BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as Escherichia coli, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., Gene 45:101 (1986); Cockett et al., Bio/Technology 8:2 (1990)).

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In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., EMBO J. 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, Nucleic Acids Res. 13:3101-3109 (1985); Van Heeke & Schuster, J. Biol. Chem. 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, Autographa californica nuclear polyhedrosis virus 30 (AcNPV) is used as a vector to express foreign genes. The virus grows in

Spodoptera frugiperda cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

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In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non- essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript,

glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

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For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991);

Tolstoshev. Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, 1993, TIB TECH 11(5):155-215); and hygro, which confers resistance to hygromycin (Santerre et al., Gene 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., J. Mol. Biol. 150:1 (1981), which are incorporated by reference herein in their entireties.

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The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., Mol. Cell. Biol. 3:257 (1983)).

The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide sequences described herein or otherwise known in the art, to facilitate purification.

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The present invention encompasses antibodies recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either in vitro or in vivo, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in in vitro immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., supra, and PCT publication WO 93/21232; EP 439,095; Naramura et al., Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); Fell et al., J. Immunol. 146:2446-2452(1991), which are incorporated by reference in their entireties.

The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody

portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or any combination of whole domains or portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991); Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337- 11341(1992) (said references incorporated by reference in their entireties).

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As discussed, supra, the polypeptides corresponding to a polypeptide. polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the in vivo half life of the polypeptides or for use in immunoassays using methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP 394,827; Traunecker et al., Nature 331:84-86 (1988). The polypeptides of the present invention fused or conjugated to an antibody having disulfide- linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995)). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP A 232,262). Alternatively, deleting the Fc part after the fusion protein has been

expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., J. Molecular Recognition 8:52-58 (1995); Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).

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Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the "HA" tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)) and the "flag" tag.

The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish

peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include 1251, 1311, 1111n or 99Tc.

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Further, an antibody or fragment thereof may be conjugated to a therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, 213Bi. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cisdichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria

toxin; a protein such as tumor necrosis factor, a-interferon, ß-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF-alpha, TNF-beta, AlM I (See, International Publication No. WO 97/33899), AlM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi et al., Int. Immunol., 6:1567-1574 (1994)), VEGI (See, International Publication No. WO 99/23105), a thrombotic agent or an antiangiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

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Techniques for conjugating such therapeutic moiety to antibodies are well known, see, e.g., Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev. 62:119-58 (1982).

Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

5 Immunophenotyping

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The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. The translation product of the gene of the present invention may be useful as a cell specific marker, or more specifically as a cellular marker that is differentially expressed at various stages of differentiation and/or maturation of particular cell types. Monoclonal antibodies directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison et al., Cell, 96:737-49 (1999)).

These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease (MRD) in acute leukemic patients) and "non-self" cells in transplantations to prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

Assays For Antibody Binding

The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays,

complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

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Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X- 100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasylol) supplemented with protein phosphatase and/or protease inhibitors (e.g., EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (e.g., 1-4 hours) at 4° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 4° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to immunoprecipitate a particular antigen can be assessed by, e.g., western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (e.g., pre-clearing the cell lysate with sepharose beads). For further discussion regarding immunoprecipitation protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.16.1.

Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (e.g., 8%- 20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human

antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g., 32P or 1251) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.8.1.

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ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion regarding ELISAs see, e.g., Ausubel et al. eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 11.2.1.

The binding affinity of an antibody to an antigen and the off-rate of an 25 antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g., 3H or 125I) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by

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scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g., 3H or 1251) in the presence of increasing amounts of an unlabeled second antibody.

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Therapeutic Uses

The present invention is further directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions described herein. The treatment and/or prevention of diseases, disorders, or conditions associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

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The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities include those with a dissociation constant or Kd less than 5 X 10⁻² M, 10⁻² M, 5 X 10⁻³ M, 10⁻³ M, 5 X 10⁻⁴ M, 10⁻⁴ M, 5 X 10⁻⁵ M, 10⁻⁵ M, 5 X 10⁻⁶ M, 10⁻⁶ M, 5 X 10⁻⁷ M, 10⁻⁷ M, 5 X 10⁻¹⁸ M, 10⁻⁸ M, 5 X 10⁻¹⁹ M, 5 X 10⁻¹⁹ M, 5 X 10⁻¹¹ M, 10⁻¹¹ M, 5 X 10⁻¹² M, 10⁻¹² M, 5 X 10⁻¹³ M, 10⁻¹³ M, 5 X 10⁻¹⁴ M, 10⁻¹⁴ M, 5 X 10⁻¹⁵ M, and 10⁻¹⁵ M.

25 Gene Therapy

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In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic

acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

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For general reviews of the methods of gene therapy, see Goldspiel et al., Clinical Pharmacy 12:488-505 (1993); Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, TIBTECH 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); and Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990).

In a preferred aspect, the compound comprises nucleic acid sequences encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989). In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid- carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids in vitro, then

transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

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In a specific embodiment, the nucleic acid sequences are directly administered in vivo, where it is expressed to produce the encoded product. accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which

facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., Biotherapy 6:291-302 (1994), which describes the use of a retroviral vector to deliver the mdrl gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., J. Clin. Invest. 93:644-651 (1994); Kiem et al., Blood 83:1467-1473 (1994); Salmons and Gunzberg, Human Gene Therapy 4:129-141 (1993); and Grossman and Wilson, Curr. Opin. in Genetics and Devel. 3:110-114 (1993).

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, Current Opinion in Genetics and Development 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., Human Gene Therapy 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., Science 252:431-434 (1991); Rosenfeld et al., Cell 68:143- 155 (1992); Mastrangeli et al., J. Clin. Invest. 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., Gene Therapy 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

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Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., Proc. Soc. Exp. Biol. Med. 204:289-300 (1993); U.S. Patent No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection

to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

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In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, Meth. Enzymol. 217:599-618 (1993); Cohen et al., Meth. Enzymol. 217:618-644 (1993); Cline, Pharmac. Ther. 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as Tlymphocytes, Blymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

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In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, Cell 71:973-985 (1992); Rheinwald, Meth. Cell Bio. 21A:229 (1980); and Pittelkow and Scott, Mayo Clinic Proc. 61:771 (1986)).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription. Demonstration of Therapeutic or Prophylactic Activity

The compounds or pharmaceutical compositions of the invention are preferably tested in vitro, and then in vivo for the desired therapeutic or prophylactic activity, prior to use in humans. For example, in vitro assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, in vitro assays which can be used to determine whether administration of a specific compound is indicated, include in vitro cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

Therapeutic/Prophylactic Administration and Composition

The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical

composition of the invention, preferably a polypeptide or antibody of the invention. In a preferred aspect, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

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Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or an immunoglobulin are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.

Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptormediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after

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surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.

In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, Science 249:1527-1533 (1990); Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, ibid., pp. 317-327; see generally ibid.)

In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, supra; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)). In another embodiment, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., Macromol. Sci. Rev. Macromol. Chem. 23:61 (1983); see also Levy et al., Science 228:190 (1985); During et al., Ann. Neurol. 25:351 (1989); Howard et al., J.Neurosurg. 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138 (1984)).

Other controlled release systems are discussed in the review by Langer (Science 249:1527-1533 (1990)).

In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by

use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox- like peptide which is known to enter the nucleus (see e.g., Joliot et al., Proc. Natl. Acad. Sci. USA 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

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The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable

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pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of

the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

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Diagnosis and Imaging

Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, or monitor diseases, disorders, and/or conditions associated with the aberrant expression and/or activity of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level.

whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of aberrant expression.

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The invention provides a diagnostic assay for diagnosing a disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

One aspect of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which specifically binds to the polypeptide of interest; b) waiting for a time interval

following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for a particular system.

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It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).

Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.

In an embodiment, monitoring of the disease or disorder is carried out by repeating the method for diagnosing the disease or disease, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.

Presence of the labeled molecule can be detected in the patient using methods known in the art for in vivo scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.

In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patent using positron emission-tomography. In yet another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

Kits

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The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody included in the kit. Preferably, the kits of the present invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate).

In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react with the polypeptide of interest. Such a kit may include a substantially isolated polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

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In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific embodiment, the antibody may be a monoclonal antibody. The detecting means of the kit may include a second, labeled monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of

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bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

Thus, the invention provides an assay system or kit for carrying out this diagnostic method. The kit generally includes a support with surface-bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

Uses of the Polynucleotides

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Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The cancer antigen polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome, thus each polynucleotide of the present invention can routinely be used as a chromosome marker using techniques known in the art.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably at least 15 bp (e.g., 15-25 bp) from the sequences shown in SEQ ID NO:X, or the complement thereto. Primers can optionally be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries, and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety).

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Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

Thus, the present invention also provides a method for chromosomal localization which involves (a) preparing PCR primers from the polynucleotide sequences in Table 3 and SEQ ID NO:X and (b) screening somatic cell hybrids containing individual chromosomes.

The polynucleotides of the present invention would likewise be useful for radiation hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g. Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London (1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton et al., Methods Cell Biol. 62:265-280 (2000); and/or Ott, J. Hered. 90:68-70 (1999) each of which is hereby incorporated by reference in its entirety.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library).) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

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Thus, once coinheritance is established, differences in a polynucleotide of the invention and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using the polynucleotides of the invention. Any of these alterations (altered expression,

chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

Thus, the invention provides a method of detecting increased or decreased expression levels of the cancer polynucleotides in affected individuals as compared to unaffected individuals using polynucleotides of the present invention and techniques known in the art, including but not limited to the method described in Example 11. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

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Thus, the invention also provides a diagnostic method useful during diagnosis of a tissue specific disorder, including cancer, involving measuring the expression level of cancer polynucleotides in tissues or other cells or body fluid from an individual and comparing the measured gene expression level with a standard cancer polynucleotide expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a tissue specific disorder.

In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject. In a general embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the invention, where each probe has one strand containing a 31'mer-end internal to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.

Where a diagnosis of a tissue specific disorder, including, for example, diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed cancer polynucleotide expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

By "measuring the expression level of cancer polynucleotides" is intended qualitatively or quantitatively measuring or estimating the level of the cancer polypeptide or the level of the mRNA encoding the cancer polypeptide in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the cancer polypeptide level or mRNA level in a second biological sample). Preferably, the cancer polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard cancer polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the tissue specific disorder or being determined by averaging levels from a population of individuals not having the tissue specific disorder. As will be appreciated in the art, once a standard cancer polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

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By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains a cancer polypeptide or the corresponding mRNA. As indicated, biological samples include body fluids (such as sputum, breast milk, vaginal pool, bile, semen, lymph, sera, plasma, urine, synovial fluid and spinal fluid) which contain the cancer polypeptide, and other tissue sources found to express the cancer polypeptide. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

The method(s) provided above may preferrably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides of the invention are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in US Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with cancer antigen polynucleotides attached may be used to identify polymorphisms between the cancer antigen polynucleotide sequences, with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e. their location, as well as, their existence) would be beneficial in

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identifying disease loci for many disorders, such as for example, in neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions. Such a method is described in US Patents 5,858,659 and 5,856,104. The US Patents referenced supra are hereby incorporated by reference in their entirety herein.

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The present invention encompasses cancer polynucleotides that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides of the invention are incorporated onto a solid support, or gene chip. For the purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by P. E. Nielsen, M. Egholm, R. H. Berg and O. Buchardt, Science 254, 1497 (1991); and M. Egholm, O. Buchardt, L.Christensen, C. Behrens, S. M. Freier, D. A. Driver, R. H. Berg, S. K. Kim, B. Norden, and P. E. Nielsen, Nature 365, 666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point (T.sub.m) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15mer duplex. Also, the absence of charge groups in PNA means that hybridization can be done at low ionic strengths and reduce possible interference by salt during the analysis.

The present invention have uses which include, but are not limited to, detecting cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia, acute myeloblastic leukemia, acute promyelocytic leukemia, acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

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Pathological cell proliferative disorders are often associated with inappropriate activation of proto-oncogenes. (Gelmann, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in Neoplastic Diseases of the Blood, Vol 1., Wiernik, P. H. et al. eds., 161-182 (1985)). Neoplasias are now believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Gelmann et al., supra) It is likely that mutated or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Gelmann et al., supra) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Gelmann et al., supra)

For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell line HL-60. When HL-60 cells are chemically induced to stop proliferation, the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580). However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-myb blocks translation of the corresponding mRNAs which downregulates expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and

differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., Proc. Natl. Acad. Sci. 85:1028 (1988); Anfossi et al., Proc. Natl. Acad. Sci. 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness is not limited to treatment of proliferative disorders of hematopoietic cells and tissues, in light of the numerous cells and cell types of varying origins which are known to exhibit proliferative phenotypes.

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In addition to the foregoing, a cancer antigen polynucleotide can be used to control gene expression through triple helix formation or through antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. Neurochem. 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance Lee et al., Nucleic Acids Research 6: 3073 (1979); Cooney et al., Science 241: 456 (1988); and Dervan et al., Science 251: 1360 (1991). Both methods rely on binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. The oligonucleotide described above can also be delivered to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of polypeptide of the present invention antigens. Both techniques are effective in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease, and in particular, for the treatment of proliferative diseases and/or conditions.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective

gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

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The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant, urine, fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on

a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to cancer polynucleotides prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

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The polynucleotides of the present invention are also useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample. Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In addition, for a number of disorders of the above tissues or cells, significantly higher or lower levels of gene expression of the polynucleotides/polypeptides of the present invention may be detected in certain tissues (e.g., tissues expressing polypeptides and/or polynucleotides of the present invention, cancer tissues and/or cancerous and/or wounded tissues) or bodily fluids (e.g., semen, vaginal pool, breast milk, bile, lymph, serum, plasma, urine, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" gene expression level, i.e., the expression level in healthy tissue from an individual not having the disorder.

Thus, the invention provides a diagnostic method of a disorder, which involves: (a) assaying gene expression level in cells or body fluid of an individual; (b) comparing the gene expression level with a standard gene expression level, whereby an increase or decrease in the assayed gene expression level compared to the standard expression level is indicative of a disorder.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

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Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

Polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays such as, for example, ABC immunoperoxidase (Hsu et al., J. Histochem. Cytochem. 29:577-580 (1981)) or cell type(s) (e.g., immunocytochemistry assays).

Antibodies can be used to assay levels of polypeptides encoded by polynucleotides of the invention in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (131 I, 125 I, 123 I, 121 I), carbon (14 C), sulfur (35 S), tritium (3 H), indium (115 m In, 113 m In, 112 In, 111 In), and technetium (99 Tc, 99 m Tc), thallium (201 Ti), gallium (68 Ga, 67 Ga), palladium (103 Pd), molybdenum (99 Mo), xenon (133 Xe), fluorine (18 F), 153 Sm, 177 Lu, 159 Gd, 149 Pm, 140 La, 175 Yb, 166 Ho, 90 Y, 47 Sc, 186 Re, 188 Re, 142 Pr, 105 Rh, 97 Ru; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying levels of polypeptide of the present invention in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

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A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, ¹³¹I, ¹¹²In, ^{99m}Tc, (¹³¹I, ¹²⁵I, ¹²³I, ¹²¹I), carbon (¹⁴C), sulfur (³⁵S), tritium (³H), indium (115mIn, 113mIn, 112In, 111In), and technetium (99Tc, 99mTc), thallium (201Ti), gallium (68Ga, 67Ga), palladium (103Pd), molybdenum (99Mo), xenon (133Xe), fluorine (18F, ¹⁵³Sm, ¹⁷⁷Lu, ¹⁵⁹Gd, ¹⁴⁹Pm, ¹⁴⁰La, ¹⁷⁵Yb, ¹⁶⁶Ho, ⁹⁰Y, ⁴⁷Sc, ¹⁸⁶Re, ¹⁸⁸Re, ¹⁴²Pr, ¹⁰⁵Rh, ⁹⁷Ru), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for immune system disorder. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of ^{99m}Tc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which express the polypeptide encoded by a polynucleotide of the invention. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or

antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

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In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

By "toxin" is meant one or more compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNAse, alpha toxin, ricin, abrin, Pseudomonas exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, 213Bi, or other radioisotopes such as, for example, ¹⁰³Pd, ¹³³Xe, ¹³¹I, ⁶⁸Ge, ⁵⁷Co, ⁶⁵Zn, ⁸⁵Sr, ³²P, ³⁵S, ⁹⁰Y, ¹⁵³Sm, ¹⁵³Gd, ¹⁶⁹Yb, ⁵¹Cr, ⁵⁴Mn, ⁷⁵Se, ¹¹³Sn, ⁹⁰Yttrium, ¹¹⁷Tin, ¹⁸⁶Rhenium, ¹⁶⁶Holmium, and ¹⁸⁸Rhenium; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

Techniques known in the art may be applied to label polypeptides of the invention (including antibodies). Such techniques include, but are not limited to, the use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361; 5,505,931; 5,489,425; 5,435,990; 5,428,139;

5,342,604; 5,274,119; 4,994,560; and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety).

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Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression level of a cancer polypeptide of the present invention in cells or body fluid of an individual; and (b) comparing the assayed polypeptide expression level with a standard polypeptide expression level, whereby an increase or decrease in the assayed polypeptide expression level compared to the standard expression level is indicative of a disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Moreover, cancer antigen polypeptides of the present invention can be used to treat or prevent diseases or conditions such as, for example, neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the activity of a polypeptide (e.g., an oncogene or tumor supressor), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease (as described supra, and elsewhere herein). For example,

administration of an antibody directed to a polypeptide of the present invention can bind, and/or neutralize the polypeptide, and/or reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

Gene Therapy Methods

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Another aspect of the present invention is to gene therapy methods for treating or preventing disorders, diseases and conditions. The gene therapy methods relate to the introduction of nucleic acid (DNA, RNA and antisense DNA or RNA) sequences into an animal to achieve expression of the polypeptide of the present invention. This method requires a polynucleotide which codes for a polypeptide of the present invention operatively linked to a promoter and any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques are known in the art, see, for example, WO90/11092, which is herein incorporated by reference.

Thus, for example, cells from a patient may be engineered with a polynucleotide (DNA or RNA) comprising a promoter operably linked to a polynucleotide of the present invention ex vivo, with the engineered cells then being provided to a patient to be treated with the polypeptide of the present invention. Such methods are well-known in the art. For example, see Belldegrun, A., et al., J. Natl. Cancer Inst. 85: 207-216 (1993); Ferrantini, M. et al., Cancer Research 53: 1107-1112 (1993); Ferrantini, M. et al., J. Immunology 153: 4604-4615 (1994); Kaido, T., et al., Int. J. Cancer 60: 221-229 (1995); Ogura, H., et al., Cancer Research 50: 5102-5106

(1990); Santodonato, L., et al., Human Gene Therapy 7:1-10 (1996); Santodonato, L., et al., Gene Therapy 4:1246-1255 (1997); and Zhang, J.-F. et al., Cancer Gene Therapy 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the artery, or through catheter injection.

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As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

In one embodiment, the polynucleotide of the present invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotide of the present invention can also be delivered in liposome formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Appropriate vectors include pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1, and pRc/CMV2 available from Invitrogen. Other suitable vectors will be readily apparent to the skilled artisan.

Any strong promoter known to those skilled in the art can be used for driving the expression of the polynucleotide sequence. Suitable promoters include adenoviral

promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible promoters, such as the MMT promoter, the metallothionein promoter; heat shock promoters; the albumin promoter; the ApoAl promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes Simplex thymidine kinase promoter; retroviral LTRs; the b-actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotide of the present invention.

Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

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The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular, fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked nucleic acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

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The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

In certain embodiments, the polynucleotide constructs are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA (1989) 86:6077-6081, which is herein incorporated by reference); and purified

transcription factors (Debs et al., J. Biol. Chem. (1990) 265:10189-10192, which is herein incorporated by reference), in functional form.

Cationic liposomes are readily available. For example, N[1-2,3-dioleyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner et al., Proc. Natl Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

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Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., P. Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol, phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphoshatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and

is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

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The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g., Straubinger et al., Methods of Immunology (1983), 101:512-527, which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include Ca2+-EDTA chelation (Papahadjopoulos et al., Biochim. Biophys. Acta (1975) 394:483; Wilson et al., Cell (1979) 17:77); ether injection (Deamer, D. and Bangham, A., Biochim. Biophys. Acta (1976) 443:629; Ostro et al., Biochem. Biophys. Res. Commun. (1977) 76:836; Fraley et al., Proc. Natl. Acad. Sci. USA (1979) 76:3348); detergent dialysis (Enoch, H. and Strittmatter, P., Proc. Natl. Acad. Sci. USA (1979) 76:145); and reverse-phase evaporation (REV) (Fraley et al., J. Biol. Chem. (1980) 255:10431; Szoka, F. and Papahadjopoulos, D., Proc. Natl. Acad. Sci.

USA (1978) 75:145; Schaefer-Ridder et al., Science (1982) 215:166), which are herein incorporated by reference.

Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 1:1. Still more preferably, the ratio will be about 1:1.

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U.S. Patent No. 5,676,954 (which is herein incorporated by reference) reports on the injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide methods for delivering DNA-cationic lipid complexes to mammals.

In certain embodiments, cells are engineered, ex vivo or in vivo, using a retroviral particle containing RNA which comprises a sequence encoding a polypeptide of the present invention. Retroviruses from which the retroviral plasmid vectors may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, Human Gene Therapy 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and CaPO₄ precipitation. In one alternative, the retroviral

plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding a polypeptide of the present invention. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either in vitro or in vivo. The transduced eukaryotic cells will express a polypeptide of the present invention.

In certain other embodiments, cells are engineered, ex vivo or in vivo, with polynucleotide contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses a polypeptide of the present invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have been used as live enteric vaccines for many years with an excellent safety profile (Schwartz, A. R. et al. (1974) Am. Rev. Respir. Dis.109:233-238). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld, M. A. et al. (1991) Science 252:431-434; Rosenfeld et al., (1992) Cell 68:143-155). Furthermore, extensive studies to attempt to establish adenovirus as a causative agent in human cancer were uniformly negative (Green, M. et al. (1979) Proc. Natl. Acad. Sci. USA 76:6606).

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Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, Curr. Opin. Genet. Devel. 3:499-503 (1993); Rosenfeld et al., Cell 68:143-155 (1992); Engelhardt et al., Human Genet. Ther. 4:759-769 (1993); Yang et al., Nature Genet. 7:362-369 (1994); Wilson et al., Nature 365:691-692 (1993); and U.S. Patent No. 5,652,224, which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express Ela and Elb, which complement the defective adenoviruses by providing the

products of the genes deleted from the vector. In addition to Ad2, other varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in one or more of all or a portion of the following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

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In certain other embodiments, the cells are engineered, ex vivo or in vivo, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper viruses to produce infectious particles (Muzyczka, N., Curr. Topics in Microbiol. Immunol. 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate precipitation, etc. Appropriate helper viruses include adenoviruses, cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct. These viral particles are then used to transduce eukaryotic cells, either ex vivo or in vivo. The transduced cells will contain the

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polynucleotide construct integrated into its genome, and will express a polypeptide of the invention.

Another method of gene therapy involves operably associating heterologous control regions and endogenous polynucleotide sequences (e.g. encoding a polypeptide of the present invention) via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

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Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5' end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can

be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

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Preferably, the polynucleotide encoding a polypeptide of the present invention contains a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide to be expressed towards or at the 5' end of the coding region. The signal sequence may be homologous or heterologous to the polynucleotide of interest and may be homologous or heterologous to the cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

15 Any mode of administration of any of the above-described polynucleotides constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., "gene guns"), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral or suppositorial solid (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers (Kaneda et al., Science 243:375 (1989)).

A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting the composition centimeters and preferably, millimeters within arteries.

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Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue inside the wound.

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Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a particular site.

Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad. Sci. USA 189:11277-11281, 1992, which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise condition requiring treatment and its severity, and the route of administration. The frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian.

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Therapeutic compositions of the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits sheep, cattle, horses and pigs, with humans being particularly preferred.

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Biological Activities

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, can be used in assays to test for one or more biological activities. If these polynucleotides or polypeptides, or agonists or antagonists of the present invention, do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides, and agonists or antagonists could be used to treat the associated disease.

15 <u>Immune Activity</u>

A polypeptide or polynucleotide, or agonists or antagonists of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. Polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of

hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

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Moreover, polynucleotides or polypeptides, or agonists or antagonists of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, polynucleotides or polypeptides, or agonists or antagonists of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.

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Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to modulate inflammation. For example, polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including chronic prostatitis, granulomatous prostatitis and malacoplakia, inflammation associated with infection (e.g., septic shock, sepsis, or

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systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

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Hyperproliferative Disorders

Polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used to treat or detect hyperproliferative disorders, including neoplasms. Polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, Polynucleotides or polypeptides, or agonists or antagonists of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by Polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to neoplasms located in the: colon, abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Examples of such hyperproliferative disorders include, but are not limited to:

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hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstron's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

One preferred embodiment utilizes polynucleotides of the present invention to inhibit aberrant cellular division, by gene therapy using the present invention, and/or protein fusions or fragments thereof.

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Thus, the present invention provides a method for treating cell proliferative disorders by inserting into an abnormally proliferating cell a polynucleotide of the present invention, wherein said polynucleotide represses said expression.

Another embodiment of the present invention provides a method of treating cell-proliferative disorders in individuals comprising administration of one or more active gene copies of the present invention to an abnormally proliferating cell or cells. In a preferred embodiment, polynucleotides of the present invention is a DNA construct comprising a recombinant expression vector effective in expressing a DNA sequence encoding said polynucleotides. In another preferred embodiment of the present invention, the DNA construct encoding the poynucleotides of the present invention is inserted into cells to be treated utilizing a retrovirus, or more preferrably an adenoviral vector (See G J. Nabel, et. al., PNAS 1999 96: 324-326, which is hereby incorporated by reference). In a most preferred embodiment, the viral vector is defective and will not transform non-proliferating cells, only proliferating cells. Moreover, in a preferred embodiment, the polynucleotides of the present invention inserted into proliferating cells either alone, or in combination with or fused to other polynucleotides, can then be modulated via an external stimulus (i.e. magnetic, specific small molecule, chemical, or drug administration, etc.), which acts upon the promoter upstream of said polynucleotides to induce expression of the encoded protein product. As such the beneficial therapeutic affect of the present invention may be expressly modulated (i.e. to increase, decrease, or inhibit expression of the present invention) based upon said external stimulus.

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Polynucleotides of the present invention may be useful in repressing expression of oncogenic genes or antigens. By "repressing expression of the oncogenic genes" is intended the suppression of the transcription of the gene, the degradation of the gene transcript (pre-message RNA), the inhibition of splicing, the destruction of the messenger RNA, the prevention of the post-translational modifications of the protein, the destruction of the protein, or the inhibition of the normal function of the protein.

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For local administration to abnormally proliferating cells, polynucleotides of the present invention may be administered by any method known to those of skill in the art including, but not limited to transfection, electroporation, microinjection of cells, or in vehicles such as liposomes, lipofectin, or as naked polynucleotides, or any other method described throughout the specification. The polynucleotide of the present invention may be delivered by known gene delivery systems such as, but not limited to, retroviral vectors (Gilboa, J. Virology 44:845 (1982); Hocke, Nature 320:275 (1986); Wilson, et al., Proc. Natl. Acad. Sci. U.S.A. 85:3014), vaccinia virus system (Chakrabarty et al., Mol. Cell Biol. 5:3403 (1985) or other efficient DNA delivery systems (Yates et al., Nature 313:812 (1985)) known to those skilled in the art. These references are exemplary only and are hereby incorporated by reference. In order to specifically deliver or transfect cells which are abnormally proliferating and spare non-dividing cells, it is preferable to utilize a retrovirus, or adenoviral (as described in the art and elsewhere herein) delivery system known to those of skill in the art. Since host DNA replication is required for retroviral DNA to integrate and the retrovirus will be unable to self replicate due to the lack of the retrovirus genes needed for its life cycle. Utilizing such a retroviral delivery system for polynucleotides of the present invention will target said gene and constructs to abnormally proliferating cells and will spare the non-dividing normal cells.

The polynucleotides of the present invention may be delivered directly to cell proliferative disorder/disease sites in internal organs, body cavities and the like by use of imaging devices used to guide an injecting needle directly to the disease site. The

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polynucleotides of the present invention may also be administered to disease sites at the time of surgical intervention.

By "cell proliferative disease" is meant any human or animal disease or disorder, affecting any one or any combination of organs, cavities, or body parts, which is characterized by single or multiple local abnormal proliferations of cells, groups of cells, or tissues, whether benign or malignant.

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Any amount of the polynucleotides of the present invention may be administered as long as it has a biologically inhibiting effect on the proliferation of the treated cells. Moreover, it is possible to administer more than one of the polynucleotide of the present invention simultaneously to the same site. By "biologically inhibiting" is meant partial or total growth inhibition as well as decreases in the rate of proliferation or growth of the cells. The biologically inhibitory dose may be determined by assessing the effects of the polynucleotides of the present invention on target malignant or abnormally proliferating cell growth in tissue culture, tumor growth in animals and cell cultures, or any other method known to one of ordinary skill in the art.

The present invention is further directed to antibody-based therapies which involve administering of anti-polypeptides and anti-polynucleotide antibodies to a mammalian, preferably human, patient for treating one or more of the described disorders. Methods for producing anti-polypeptides and anti-polynucleotide antibodies polyclonal and monoclonal antibodies are described in detail elsewhere herein. Such antibodies may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of

the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

In particular, the antibodies, fragments and derivatives of the present invention are useful for treating a subject having or developing cell proliferative and/or differentiation disorders as described herein. Such treatment comprises administering a single or multiple doses of the antibody, or a fragment, derivative, or a conjugate thereof.

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The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors, for example., which serve to increase the number or activity of effector cells which interact with the antibodies.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragements thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides, including fragements thereof. Preferred binding affinities include those with a dissociation constant or Kd less than 5X10⁻⁶M, 10⁻⁶M, 5X10⁻⁷M, 10⁻⁷M, 5X10⁻⁸M, 10⁻⁸M, 5X10⁻⁹M, 10⁻⁹M, 5X10⁻¹⁰M, 10⁻¹⁰M, 5X10⁻¹¹M, 5X10⁻¹²M, 5X10⁻¹³M, 10⁻¹³M, 5X10⁻¹⁴M, 5X10⁻¹⁵M, and 10⁻¹⁵M.

Moreover, polypeptides of the present invention are useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere herein. In a most preferred embodiment, said anti-angiogenesis effect may be achieved indirectly, for example, through the inhibition of hematopoietic, tumor-specific cells, such as tumor-associated macrophages (See Joseph IB, et al. J Natl Cancer Inst, 90(21):1648-53 (1998), which is hereby incorporated by reference). Antibodies directed to polypeptides or polynucleotides of the present invention may also result in inhibition of angiogenesis directly, or indirectly (See Witte L, et al.,

Cancer Metastasis Rev. 17(2):155-61 (1998), which is hereby incorporated by reference)).

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Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a deathdomain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1). TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (See Schulze-Osthoff K, et.al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuviants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, Mutat Res 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem Biol Interact. Apr 24;111-112:23-34 (1998), J Mol Med.76(6):402-12 (1998), Int J Tissue React; 20(1):3-15 (1998), which are all hereby incorporated by reference).

Polypeptides, including protein fusions to, or fragments thereof, of the present invention are useful in inhibiting the metastasis of proliferative cells or tissues. Inhibition may occur as a direct result of administering polypeptides, or antibodies directed to said polypeptides as described elsewere herein, or indirectly, such as activating the expression of proteins known to inhibit metastasis, for example alpha 4 integrins, (See, e.g., Curr Top Microbiol Immunol 1998;231:125-41, which is hereby incorporated by reference). Such thereapeutic affects of the present invention may be achieved either alone, or in combination with small molecule drugs or adjuvants.

In another embodiment, the invention provides a method of delivering compositions containing the polypeptides of the invention (e.g., compositions containing polypeptides or polypeptide antibodes associated with heterologous

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polypeptides, heterologous nucleic acids, toxins, or prodrugs) to targeted cells expressing the polypeptide of the present invention. Polypeptides or polypeptide antibodes of the invention may be associated with with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. Polypeptides, protein fusions to, or fragments thereof, of the present invention are useful in enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues, either directly, such as would occur if the polypeptides of the present invention 'vaccinated' the immune response to respond to proliferative antigens and immunogens, or indirectly, such as in activating the expression of proteins known to enhance the immune response (e.g. chemokines), to said antigens and immunogens.

Cardiovascular Disorders

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Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat cardiovascular disorders, including peripheral artery disease, such as limb ischemia.

Cardiovascular disorders include cardiovascular abnormalities, such as arterioarterial fistula, arteriovenous fistula, cerebral arteriovenous malformations, congenital
heart defects, pulmonary atresia, and Scimitar Syndrome. Congenital heart defects
include aortic coarctation, cor triatriatum, coronary vessel anomalies, crisscross heart,
dextrocardia, patent ductus arteriosus, Ebstein's anomaly, Eisenmenger complex,
hypoplastic left heart syndrome, levocardia, tetralogy of fallot, transposition of great
vessels, double outlet right ventricle, tricuspid atresia, persistent truncus arteriosus,
and heart septal defects, such as aortopulmonary septal defect, endocardial cushion
defects, Lutembacher's Syndrome, trilogy of Fallot, ventricular heart septal defects.

Cardiovascular disorders also include heart disease, such as arrhythmias, carcinoid heart disease, high cardiac output, low cardiac output, cardiac tamponade, endocarditis (including bacterial), heart aneurysm, cardiac arrest, congestive heart failure, congestive cardiomyopathy, paroxysmal dyspnea, cardiac edema, heart hypertrophy, congestive cardiomyopathy, left ventricular hypertrophy, right

ventricular hypertrophy, post-infarction heart rupture, ventricular septal rupture, heart valve diseases, myocardial diseases, myocardial ischemia, pericardial effusion, pericarditis (including constrictive and tuberculous), pneumopericardium, postpericardiotomy syndrome, pulmonary heart disease, rheumatic heart disease, ventricular dysfunction, hyperemia, cardiovascular pregnancy complications, Scimitar Syndrome, cardiovascular syphilis, and cardiovascular tuberculosis.

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Arrhythmias include sinus arrhythmia, atrial fibrillation, atrial flutter, bradycardia, extrasystole, Adams-Stokes Syndrome, bundle-branch block, sinoatrial block, long QT syndrome, parasystole, Lown-Ganong-Levine Syndrome, Mahaimtype pre-excitation syndrome, Wolff-Parkinson-White syndrome, sick sinus syndrome, tachycardias, and ventricular fibrillation. Tachycardias include paroxysmal tachycardia, supraventricular tachycardia, accelerated idioventricular rhythm, atrioventricular nodal reentry tachycardia, ectopic atrial tachycardia, ectopic junctional tachycardia, sinoatrial nodal reentry tachycardia, sinus tachycardia, Torsades de Pointes, and ventricular tachycardia.

Heart valve disease include aortic valve insufficiency, aortic valve stenosis, hear murmurs, aortic valve prolapse, mitral valve prolapse, tricuspid valve prolapse, mitral valve insufficiency, mitral valve stenosis, pulmonary atresia, pulmonary valve insufficiency, pulmonary valve stenosis, tricuspid atresia, tricuspid valve insufficiency, and tricuspid valve stenosis.

Myocardial diseases include alcoholic cardiomyopathy, congestive cardiomyopathy, hypertrophic cardiomyopathy, aortic subvalvular stenosis, pulmonary subvalvular stenosis, restrictive cardiomyopathy, Chagas cardiomyopathy, endocardial fibroelastosis, endomyocardial fibrosis, Kearns Syndrome, myocardial reperfusion injury, and myocarditis.

Myocardial ischemias include coronary disease, such as angina pectoris, coronary aneurysm, coronary arteriosclerosis, coronary thrombosis, coronary vasospasm, myocardial infarction and myocardial stunning.

Cardiovascular diseases also include vascular diseases such as aneurysms, angiodysplasia, angiomatosis, bacillary angiomatosis, Hippel-Lindau Disease,

Klippel-Trenaunay-Weber Syndrome. Sturge-Weber Syndrome, angioneurotic edema, aortic diseases, Takayasu's Arteritis, aortitis, Leriche's Syndrome, arterial occlusive diseases, arteritis, enarteritis, polyarteritis nodosa, cerebrovascular disorders, diabetic angiopathies, diabetic retinopathy, embolisms, thrombosis, erythromelalgia, hemorrhoids, hepatic veno-occlusive disease, hypertension, hypotension, ischemia, peripheral vascular diseases, phlebitis, pulmonary veno-occlusive disease, Raynaud's disease, CREST syndrome, retinal vein occlusion, Scimitar syndrome, superior vena cava syndrome, telangiectasia, atacia telangiectasia, hereditary hemorrhagic telangiectasia, varicocele, varicose veins, varicose ulcer, vasculitis, and venous insufficiency.

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Aneurysms include dissecting aneurysms, false aneurysms, infected aneurysms, ruptured aneurysms, aortic aneurysms, cerebral aneurysms, coronary aneurysms, heart aneurysms, and iliac aneurysms.

Arterial occlusive diseases include arteriosclerosis, intermittent claudication, carotid stenosis, fibromuscular dysplasias, mesenteric vascular occlusion, Moyamoya disease, renal artery obstruction, retinal artery occlusion, and thromboangiitis obliterans.

Cerebrovascular disorders include carotid artery diseases, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformation, cerebral artery diseases, cerebral embolism and thrombosis, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, cerebral hemorrhage, epidural hematoma, subdural hematoma, subaraxhnoid hemorrhage, cerebral infarction, cerebral ischemia (including transient), subclavian steal syndrome, periventricular leukomalacia, vascular headache, cluster headache, migraine, and vertebrobasilar insufficiency.

Embolisms include air embolisms, amniotic fluid embolisms, cholesterol embolisms, blue toe syndrome, fat embolisms, pulmonary embolisms, and thromoboembolisms. Thrombosis include coronary thrombosis, hepatic vein thrombosis, retinal vein occlusion, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, and thrombophlebitis.

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Ischemia includes cerebral ischemia, ischemic colitis, compartment syndromes, anterior compartment syndrome, myocardial ischemia, reperfusion injuries, and peripheral limb ischemia. Vasculitis includes aortitis, arteritis, Behcet's Syndrome, Churg-Strauss Syndrome, mucocutaneous lymph node syndrome, thromboangiitis obliterans, hypersensitivity vasculitis, Schoenlein-Henoch purpura, allergic cutaneous vasculitis, and Wegener's granulomatosis.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, are especially effective for the treatment of critical limb ischemia and coronary disease.

Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators, gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppositorial solid pharmaceutical formulations, decanting or topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

20 Anti-Angiogenesis Activity

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The naturally occurring balance between endogenous stimulators and inhibitors of angiogenesis is one in which inhibitory influences predominate. Rastinejad et al., Cell 56:345-355 (1989). In those rare instances in which neovascularization occurs under normal physiological conditions, such as wound healing, organ regeneration, embryonic development, and female reproductive processes, angiogenesis is stringently regulated and spatially and temporally delimited. Under conditions of pathological angiogenesis such as that characterizing solid tumor growth, these regulatory controls fail. Unregulated angiogenesis becomes pathologic and sustains progression of many neoplastic and non-neoplastic diseases. A number of serious diseases are dominated by abnormal neovascularization

including solid tumor growth and metastases, arthritis, some types of eye disorders, and psoriasis. See, e.g., reviews by Moses et al., Biotech. 9:630-634 (1991); Folkman et al., N. Engl. J. Med., 333:1757-1763 (1995); Auerbach et al., J. Microvasc. Res. 29:401-411 (1985); Folkman, Advances in Cancer Research, eds. Klein and Weinhouse, Academic Press, New York, pp. 175-203 (1985); Patz, Am. J. Opthalmol. 94:715-743 (1982); and Folkman et al., Science 221:719-725 (1983). In a number of pathological conditions, the process of angiogenesis contributes to the disease state. For example, significant data have accumulated which suggest that the growth of solid tumors is dependent on angiogenesis. Folkman and Klagsbrun, Science 235:442-447 (1987).

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The polynucleotides encoding a polypeptide of the present invention may be administered along with other polynucleotides encoding an angiogenic protein. Examples of angiogenic proteins include, but are not limited to, acidic and basic fibroblast growth factors, VEGF-1, VEGF-2, VEGF-3, epidermal growth factor alpha and beta, platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor alpha, hepatocyte growth factor, insulin like growth factor, colony stimulating factor, macrophage colony stimulating factor, granulocyte/macrophage colony stimulating factor, and nitric oxide synthase.

The present invention provides for treatment of diseases or disorders associated with neovascularization by administration of the polynucleotides and/or polypeptides of the invention, as well as agonists or antagonists of the present invention. Malignant and metastatic conditions which can be treated with the polynucleotides and polypeptides, or agonists or antagonists of the invention include, but are not limited to, malignancies, solid tumors, and cancers described herein and otherwise known in the art (for a review of such disorders, see Fishman et al., Medicine, 2d Ed., J. B. Lippincott Co., Philadelphia (1985)). Thus, the present invention provides a method of treating an angiogenesis-related disease and/or disorder, comprising administering to an individual in need thereof a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist of the invention. For example, polynucleotides, polypeptides, antagonists and/or agonists

may be utilized in a variety of additional methods in order to therapeutically treat a cancer or tumor. Cancers which may be treated with polynucleotides, polypeptides, antagonists and/or agonists include, but are not limited to solid tumors, including prostate, lung, breast, ovarian, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer; primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non- small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias. For example, polynucleotides, polypeptides, antagonists and/or agonists may be delivered topically, in order to treat cancers such as skin cancer, head and neck tumors, breast tumors, and Kaposi's sarcoma.

Within yet other aspects, polynucleotides, polypeptides, antagonists and/or agonists may be utilized to treat superficial forms of bladder cancer by, for example, intravesical administration. Polynucleotides, polypeptides, antagonists and/or agonists may be delivered directly into the tumor, or near the tumor site, via injection or a catheter. Of course, as the artisan of ordinary skill will appreciate, the appropriate mode of administration will vary according to the cancer to be treated. Other modes of delivery are discussed herein.

Polynucleotides, polypeptides, antagonists and/or agonists may be useful in treating other disorders, besides cancers, which involve angiogenesis. These disorders include, but are not limited to: benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; artheroscleric plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uvietis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization;

telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis.

For example, within one aspect of the present invention methods are provided for treating hypertrophic scars and keloids, comprising the step of administering a polynucleotide, polypeptide, antagonist and/or agonist of the invention to a hypertrophic scar or keloid.

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Within one embodiment of the present invention polynucleotides, polypeptides, antagonists and/or agonists are directly injected into a hypertrophic scar or keloid, in order to prevent the progression of these lesions. This therapy is of particular value in the prophylactic treatment of conditions which are known to result in the development of hypertrophic scars and keloids (e.g., burns), and is preferably initiated after the proliferative phase has had time to progress (approximately 14 days after the initial injury), but before hypertrophic scar or keloid development. As noted above, the present invention also provides methods for treating neovascular diseases of the eye, including for example, corneal neovascularization, neovascular glaucoma, proliferative diabetic retinopathy, retrolental fibroplasia and macular degeneration.

Moreover, Ocular disorders associated with neovascularization which can be treated with the polynucleotides and polypeptides of the present invention (including agonists and/or antagonists) include, but are not limited to: neovascular glaucoma, diabetic retinopathy, retinoblastoma, retrolental fibroplasia, uveitis, retinopathy of prematurity macular degeneration, corneal graft neovascularization, as well as other eye inflammatory diseases, ocular tumors and diseases associated with choroidal or iris neovascularization. See, e.g., reviews by Waltman et al., Am. J. Ophthal. 85:704-710 (1978) and Gartner et al., Surv. Ophthal. 22:291-312 (1978).

Thus, within one aspect of the present invention methods are provided for treating neovascular diseases of the eye such as comeal neovascularization (including corneal graft neovascularization), comprising the step of administering to a patient a therapeutically effective amount of a compound (as described above) to the cornea, such that the formation of blood vessels is inhibited. Briefly, the cornea is a tissue which normally lacks blood vessels. In certain pathological conditions however,

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capillaries may extend into the cornea from the pericorneal vascular plexus of the limbus. When the cornea becomes vascularized, it also becomes clouded, resulting in a decline in the patient's visual acuity. Visual loss may become complete if the cornea completely opacitates. A wide variety of disorders can result in corneal neovascularization, including for example, corneal infections (e.g., trachoma, herpes simplex keratitis, leishmaniasis and onchocerciasis), immunological processes (e.g., graft rejection and Stevens-Johnson's syndrome), alkali burns, trauma, inflammation (of any cause), toxic and nutritional deficiency states, and as a complication of wearing contact lenses.

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Within particularly preferred embodiments of the invention, may be prepared for topical administration in saline (combined with any of the preservatives and antimicrobial agents commonly used in ocular preparations), and administered in eyedrop form. The solution or suspension may be prepared in its pure form and administered several times daily. Alternatively, anti-angiogenic compositions, prepared as described above, may also be administered directly to the cornea. Within preferred embodiments, the anti-angiogenic composition is prepared with a muco-adhesive polymer which binds to cornea. Within further embodiments, the anti-angiogenic factors or anti-angiogenic compositions may be utilized as an adjunct to conventional steroid therapy. Topical therapy may also be useful prophylactically in corneal lesions which are known to have a high probability of inducing an angiogenic response (such as chemical burns). In these instances the treatment, likely in combination with steroids, may be instituted immediately to help prevent subsequent complications.

Within other embodiments, the compounds described above may be injected directly into the corneal stroma by an ophthalmologist under microscopic guidance. The preferred site of injection may vary with the morphology of the individual lesion, but the goal of the administration would be to place the composition at the advancing front of the vasculature (i.e., interspersed between the blood vessels and the normal cornea). In most cases this would involve perilimbic corneal injection to "protect" the cornea from the advancing blood vessels. This method may also be utilized shortly

after a corneal insult in order to prophylactically prevent corneal neovascularization. In this situation the material could be injected in the perilimbic cornea interspersed between the corneal lesion and its undesired potential limbic blood supply. Such methods may also be utilized in a similar fashion to prevent capillary invasion of transplanted corneas. In a sustained-release form injections might only be required 2-3 times per year. A steroid could also be added to the injection solution to reduce inflammation resulting from the injection itself.

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Within another aspect of the present invention, methods are provided for treating neovascular glaucoma, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. In one embodiment, the compound may be administered topically to the eye in order to treat early forms of neovascular glaucoma. Within other embodiments, the compound may be implanted by injection into the region of the anterior chamber angle. Within other embodiments, the compound may also be placed in any location such that the compound is continuously released into the aqueous humor. Within another aspect of the present invention, methods are provided for treating proliferative diabetic retinopathy, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eyes, such that the formation of blood vessels is inhibited.

Within particularly preferred embodiments of the invention, proliferative diabetic retinopathy may be treated by injection into the aqueous humor or the vitreous, in order to increase the local concentration of the polynucleotide, polypeptide, antagonist and/or agonist in the retina. Preferably, this treatment should be initiated prior to the acquisition of severe disease requiring photocoagulation.

Within another aspect of the present invention, methods are provided for treating retrolental fibroplasia, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. The

compound may be administered topically, via intravitreous injection and/or via intraocular implants.

Additionally, disorders which can be treated with the polynucleotides, polypeptides, agonists and/or agonists include, but are not limited to, hemangioma, arthritis, psoriasis, angiofibroma, atherosclerotic plaques, delayed wound healing, granulations, hemophilic joints, hypertrophic scars, nonunion fractures, Osler-Weber syndrome, pyogenic granuloma, scleroderma, trachoma, and vascular adhesions.

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Moreover, disorders and/or states, which can be treated with be treated with the the polynucleotides, polypeptides, agonists and/or agonists include, but are not limited to, solid tumors, blood born tumors such as leukemias, tumor metastasis, Kaposi's sarcoma, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas, rheumatoid arthritis, psoriasis, ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, and uvietis, delayed wound healing, endometriosis, vascluogenesis, granulations, hypertrophic scars (keloids), nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma fibromuscular dysplasia, wound granulation, Crohn's disease, atherosclerosis, birth control agent by preventing vascularization required for embryo implantation controlling menstruation, diseases that have angiogenesis as a pathologic consequence such as cat scratch disease (Rochele minalia quintosa), ulcers (Helicobacter pylori), Bartonellosis and bacillary angiomatosis.

In one aspect of the birth control method, an amount of the compound sufficient to block embryo implantation is administered before or after intercourse and fertilization have occurred, thus providing an effective method of birth control, possibly a "morning after" method. Polynucleotides, polypeptides, agonists and/or agonists may also be used in controlling menstruation or administered as either a

peritoneal lavage fluid or for peritoneal implantation in the treatment of endometriosis.

Polynucleotides, polypeptides, agonists and/or agonists of the present invention may be incorporated into surgical sutures in order to prevent stitch granulomas.

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Polynucleotides, polypeptides, agonists and/or agonists may be utilized in a wide variety of surgical procedures. For example, within one aspect of the present invention a compositions (in the form of, for example, a spray or film) may be utilized to coat or spray an area prior to removal of a tumor, in order to isolate normal surrounding tissues from malignant tissue, and/or to prevent the spread of disease to surrounding tissues. Within other aspects of the present invention, compositions (e.g., in the form of a spray) may be delivered via endoscopic procedures in order to coat tumors, or inhibit angiogenesis in a desired locale. Within yet other aspects of the present invention, surgical meshes which have been coated with anti- angiogenic compositions of the present invention may be utilized in any procedure wherein a surgical mesh might be utilized. For example, within one embodiment of the invention a surgical mesh laden with an anti-angiogenic composition may be utilized during abdominal cancer resection surgery (e.g., subsequent to colon resection) in order to provide support to the structure, and to release an amount of the anti-angiogenic factor.

Within further aspects of the present invention, methods are provided for treating tumor excision sites, comprising administering a polynucleotide, polypeptide, agonist and/or agonist to the resection margins of a tumor subsequent to excision, such that the local recurrence of cancer and the formation of new blood vessels at the site is inhibited. Within one embodiment of the invention, the anti-angiogenic compound is administered directly to the tumor excision site (e.g., applied by swabbing, brushing or otherwise coating the resection margins of the tumor with the anti-angiogenic compound). Alternatively, the anti-angiogenic compounds may be incorporated into known surgical pastes prior to administration. Within particularly

preferred embodiments of the invention, the anti-angiogenic compounds are applied after hepatic resections for malignancy, and after neurosurgical operations.

Within one aspect of the present invention, polynucleotides, polypeptides, agonists and/or agonists may be administered to the resection margin of a wide variety of tumors, including for example, breast, colon, brain and hepatic tumors. For example, within one embodiment of the invention, anti-angiogenic compounds may be administered to the site of a neurological tumor subsequent to excision, such that the formation of new blood vessels at the site are inhibited.

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The polynucleotides, polypeptides, agonists and/or agonists of the present invention may also be administered along with other anti-angiogenic factors. Representative examples of other anti-angiogenic factors include: Anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel, Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo

molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

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A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells). (Murata et al., Cancer Res. 51:22-26, 1991); Sulphated Polysaccharide Peptidoglycan Complex (SP-PG) (the function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cishydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin; Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio. Chem. 267:17321-17326, 1992); Chymostatin (Tomkinson et al., Biochem J. 286:475-480, 1992); Cyclodextrin Tetradecasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557, 1990); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446, 1987); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664, 1987); Bisantrene (National Cancer Institute); Lobenzarit disodium (N-(2)-carboxyphenyl-4chloroanthronilic acid disodium or "CCA"; Takeuchi et al., Agents Actions 36:312-316, 1992); Thalidomide; Angostatic steroid; AGM-1470; carboxynaminolmidazole; and metalloproteinase inhibitors such as BB94.

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Diseases at the Cellular Level

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Diseases associated with increased cell survival or the inhibition of apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as antagonists or agonists of the present invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection. In preferred embodiments, polynucleotides, polypeptides, and/or antagonists of the invention are used to inhibit growth, progression, and/or metasis of cancers, in particular those listed above.

Additional diseases or conditions associated with increased cell survival that could be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma,

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lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma, and retinoblastoma.

Diseases associated with increased apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, include AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestosis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

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Wound Healing and Epithelial Cell Proliferation

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate epithelial cell proliferation and basal keratinocytes for the purpose of wound

healing, and to stimulate hair follicle production and healing of dermal wounds. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may be clinically useful in stimulating wound healing including surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associted with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote dermal reestablishment subsequent to dermal loss

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to increase the adherence of skin grafts to a wound bed and to stimulate re-epithelialization from the wound bed. The following are types of grafts that polynucleotides or polypeptides, agonists or antagonists of the present invention, could be used to increase adherence to a wound bed: autografts, artificial skin, allografts, autodermic graft, autoepdermic grafts, avacular grafts, Blair-Brown grafts, bone graft, brephoplastic grafts, cutis graft, delayed graft, dermic graft, epidermic graft, fascia graft, full thickness graft, heterologous graft, xenograft, homologous graft, hyperplastic graft, lamellar graft, mesh graft, mucosal graft, Ollier-Thiersch graft, omenpal graft, patch graft, pedicle graft, penetrating graft, split skin graft, thick split graft. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, can be used to promote skin strength and to improve the appearance of aged skin.

It is believed that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, will also produce changes in hepatocyte proliferation, and epithelial cell proliferation in the lung, breast, pancreas, stomach, small intesting, and large intestine. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could promote proliferation of

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epithelial cells such as sebocytes, hair follicles, hepatocytes, type II pneumocytes, mucin-producing goblet cells, and other epithelial cells and their progenitors contained within the skin, lung, liver, and gastrointestinal tract. Polynucleotides or polypeptides, agonists or antagonists of the present invention, may promote proliferation of endothelial cells, keratinocytes, and basal keratinocytes.

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Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to reduce the side effects of gut toxicity that result from radiation, chemotherapy treatments or viral infections. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may have a cytoprotective effect on the small intestine mucosa. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may also stimulate healing of mucositis (mouth ulcers) that result from chemotherapy and viral infections.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could further be used in full regeneration of skin in full and partial thickness skin defects, including burns, (i.e., repopulation of hair follicles, sweat glands, and sebaceous glands), treatment of other skin defects such as psoriasis. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat epidermolysis bullosa, a defect in adherence of the epidermis to the underlying dermis which results in frequent, open and painful blisters by accelerating reepithelialization of these lesions. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to treat gastric and doudenal ulcers and help heal by scar formation of the mucosal lining and regeneration of glandular mucosa and duodenal mucosal lining more rapidly. Inflamamatory bowel diseases, such as Crohn's disease and ulcerative colitis, are diseases which result in destruction of the mucosal surface of the small or large intestine, respectively. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote the resurfacing of the mucosal surface to aid more rapid healing and to prevent progression of inflammatory bowel disease. Treatment with polynucleotides or polypeptides, agonists or antagonists of the present invention, is expected to have a significant effect on the

production of mucus throughout the gastrointestinal tract and could be used to protect the intestinal mucosa from injurious substances that are ingested or following surgery. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat diseases associate with the under expression.

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Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to prevent and heal damage to the lungs due to various pathological states. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, which could stimulate proliferation and differentiation and promote the repair of alveoli and brochiolar epithelium to prevent or treat acute or chronic lung damage. For example, emphysema, which results in the progressive loss of aveoli, and inhalation injuries, i.e., resulting from smoke inhalation and burns, that cause necrosis of the bronchiolar epithelium and alveoli could be effectively treated using polynucleotides or polypeptides, agonists or antagonists of the present invention. Also, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to stimulate the proliferation of and differentiation of type II pneumocytes, which may help treat or

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could stimulate the proliferation and differentiation of hepatocytes and, thus, could be used to alleviate or treat liver diseases and pathologies such as fulminant liver failure caused by cirrhosis, liver damage caused by viral hepatitis and toxic substances (i.e., acetaminophen, carbon tetraholoride and other hepatotoxins known in the art).

prevent disease such as hyaline membrane diseases, such as infant respiratory distress

syndrome and bronchopulmonary displasia, in premature infants.

In addition, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to maintain the islet function so as to alleviate, delay or prevent permanent manifestation of the disease. Also, polynucleotides or

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polypeptides, as well as agonists or antagonists of the present invention, could be used as an auxiliary in islet cell transplantation to improve or promote islet cell function.

5 Neurological Diseases

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In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate neurological cell proliferation and/or differentiation. Therefore, polynucleotides, polypeptides, agonists and/or antagonists of the invention may be used to treat and/or detect neurologic diseases. Moreover, polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used as a marker or detector of a particular nervous system disease or disorder.

Examples of neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include brain diseases, such as metabolic brain diseases which includes phenylketonuria such as maternal phenylketonuria, pyruvate carboxylase deficiency, pyruvate dehydrogenase complex deficiency, Wernicke's Encephalopathy, brain edema, brain neoplasms such as cerebellar neoplasms which include infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms. hypothalamic neoplasms, supratentorial neoplasms, canavan disease, cerebellar diseases such as cerebellar ataxia which include spinocerebellar degeneration such as ataxia telangiectasia, cerebellar dyssynergia, Friederich's Ataxia, Machado-Joseph Disease, olivopontocerebellar atrophy, cerebellar neoplasms such as infratentorial neoplasms, diffuse cerebral sclerosis such as encephalitis periaxialis, globoid cell leukodystrophy, metachromatic leukodystrophy and subacute sclerosing panencephalitis, cerebrovascular disorders (such as carotid artery diseases which include carotid artery thrombosis, carotid stenosis and Moyamoya Disease, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformations, cerebral artery diseases, cerebral embolism and

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thrombosis such as carotid artery thrombosis, sinus thrombosis and Wallenberg's Syndrome, cerebral hemorrhage such as epidural hematoma, subdural hematoma and subarachnoid hemorrhage, cerebral infarction, cerebral ischemia such as transient cerebral ischemia, Subclavian Steal Syndrome and vertebrobasilar insufficiency. vascular dementia such as multi-infarct dementia, periventricular leukomalacia, vascular headache such as cluster headache, migraine, dementia such as AIDS Dementia Complex, presentile dementia such as Alzheimer's Disease and Creutzfeldt-Jakob Syndrome, senile dementia such as Alzheimer's Disease and progressive supranuclear palsy, vascular dementia such as multi-infarct dementia, encephalitis which include encephalitis periaxialis, viral encephalitis such as epidemic encephalitis, Japanese Encephalitis, St. Louis Encephalitis, tick-borne encephalitis and West Nile Fever, acute disseminated encephalomyelitis, meningoencephalitis such as uveomeningoencephalitic syndrome, Postencephalitic Parkinson Disease and subacute sclerosing panencephalitis, encephalomalacia such as periventricular leukomalacia, epilepsy such as generalized epilepsy which includes infantile spasms. absence epilepsy, myoclonic epilepsy which includes MERRF Syndrome, tonicclonic epilepsy, partial epilepsy such as complex partial epilepsy, frontal lobe epilepsy and temporal lobe epilepsy, post-traumatic epilepsy, status epilepticus such as Epilepsia Partialis Continua, Hallervorden-Spatz Syndrome, hydrocephalus such as Dandy-Walker Syndrome and normal pressure hydrocephalus, hypothalamic diseases such as hypothalamic neoplasms, cerebral malaria, narcolepsy which includes cataplexy, bulbar poliomyelitis, cerebri pseudotumor, Rett Syndrome, Reye's Syndrome, thalamic diseases, cerebral toxoplasmosis, intracranial tuberculoma and Zellweger Syndrome, central nervous system infections such as AIDS Dementia Complex, Brain Abscess, subdural empyema, encephalomyelitis such as Equine Encephalomyelitis, Venezuelan Equine Encephalomyelitis, Necrotizing Hemorrhagic Encephalomyelitis, Visna, cerebral malaria, meningitis such as arachnoiditis, aseptic meningtitis such as viral meningtitis which includes lymphocytic choriomeningitis. Bacterial meningtitis which includes Haemophilus Meningtitis, Listeria Meningtitis, Meningococcal Meningtitis such as Waterhouse-Friderichsen Syndrome,

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Pneumococcal Meningtitis and meningeal tuberculosis, fungal meningitis such as Cryptococcal Meningtitis, subdural effusion, meningoencephalitis such as uvemeningoencephalitic syndrome, myelitis such as transverse myelitis, neurosyphilis such as tabes dorsalis, poliomyelitis which includes bulbar poliomyelitis and postpoliomyelitis syndrome, prion diseases (such as Creutzfeldt-Jakob Syndrome, Bovine Spongiform Encephalopathy, Gerstmann-Straussler Syndrome, Kuru, Scrapie) cerebral toxoplasmosis, central nervous system neoplasms such as brain neoplasms that include cerebellear neoplasms such as infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms and supratentorial neoplasms, meningeal neoplasms, spinal cord neoplasms which include epidural neoplasms, demyelinating diseases such as Canavan Diseases, diffuse cerebral sceloris which includes adrenoleukodystrophy, encephalitis periaxialis, globoid cell leukodystrophy, diffuse cerebral sclerosis such as metachromatic leukodystrophy, allergic encephalomyelitis, necrotizing hemorrhagic encephalomyelitis, progressive multifocal leukoencephalopathy, multiple sclerosis, central pontine myelinolysis, transverse myelitis, neuromyelitis optica, Scrapie, Swayback, Chronic Fatigue Syndrome, Visna, High Pressure Nervous Syndrome, Meningism, spinal cord diseases such as amyotonia congenita, amyotrophic lateral sclerosis, spinal muscular atrophy such as Werdnig-Hoffmann Disease, spinal cord compression, spinal cord neoplasms such as epidural neoplasms, syringomyelia, Tabes Dorsalis, Stiff-Man Syndrome, mental retardation such as Angelman Syndrome, Cri-du-Chat Syndrome, De Lange's Syndrome, Down Syndrome, Gangliosidoses such as gangliosidoses G(M1), Sandhoff Disease, Tay-Sachs Disease, Hartnup Disease, homocystinuria, Laurence-Moon- Biedl Syndrome, Lesch-Nyhan Syndrome, Maple Syrup Urine Disease, mucolipidosis such as fucosidosis, neuronal ceroid-lipofuscinosis, oculocerebrorenal syndrome, phenylketonuria such as maternal phenylketonuria, Prader-Willi Syndrome, Rett Syndrome, Rubinstein-Taybi Syndrome, Tuberous Sclerosis, WAGR Syndrome, nervous system abnormalities such as holoprosencephaly, neural tube defects such as anencephaly which includes hydrangencephaly, Arnold-Chairi Deformity, encephalocele, meningocele,

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meningomyelocele, spinal dysraphism such as spina bifida cystica and spina bifida occulta, hereditary motor and sensory neuropathies which include Charcot-Marie Disease, Hereditary optic atrophy, Refsum's Disease, hereditary spastic paraplegia, Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies such as Congenital Analgesia and Familial Dysautonomia, Neurologic manifestations (such as agnosia that include Gerstmann's Syndrome, Amnesia such as retrograde amnesia, apraxia, neurogenic bladder, cataplexy, communicative disorders such as hearing disorders that includes deafness, partial hearing loss, loudness recruitment and tinnitus, language disorders such as aphasia which include agraphia, anomia, broca aphasia, and Wernicke Aphasia, Dyslexia such as Acquired Dyslexia, language development disorders, speech disorders such as aphasia which includes anomia, broca aphasia and Wernicke Aphasia, articulation disorders, communicative disorders such as speech disorders which include dysarthria, echolalia, mutism and stuttering, voice disorders such as aphonia and hoarseness, decerebrate state, delirium. fasciculation, hallucinations, meningism, movement disorders such as angelman syndrome, ataxia, athetosis, chorea, dystonia, hypokinesia, muscle hypotonia, myoclonus, tic, torticollis and tremor, muscle hypertonia such as muscle rigidity such as stiff-man syndrome, muscle spasticity, paralysis such as facial paralysis which includes Herpes Zoster Oticus, Gastroparesis, Hemiplegia, ophthalmoplegia such as diplopia, Duane's Syndrome, Horner's Syndrome, Chronic progressive external ophthalmoplegia such as Kearns Syndrome, Bulbar Paralysis, Tropical Spastic Paraparesis, Paraplegia such as Brown-Sequard Syndrome, quadriplegia, respiratory paralysis and vocal cord paralysis, paresis, phantom limb, taste disorders such as ageusia and dysgeusia, vision disorders such as amblyopia, blindness, color vision defects, diplopia, hemianopsia, scotoma and subnormal vision, sleep disorders such as hypersomnia which includes Kleine-Levin Syndrome, insomnia, and somnambulism, spasm such as trismus, unconsciousness such as coma, persistent vegetative state and syncope and vertigo, neuromuscular diseases such as amyotonia congenita, amyotrophic lateral sclerosis, Lambert-Eaton Myasthenic Syndrome, motor neuron disease, muscular atrophy such as spinal muscular atrophy, Charcot-Marie Disease

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and Werdnig-Hoffmann Disease, Postpoliomyelitis Syndrome, Muscular Dystrophy, Myasthenia Gravis, Myotonia Atrophica, Myotonia Confenita, Nemaline Myopathy, Familial Periodic Paralysis, Multiplex Paramyloclonus, Tropical Spastic Paraparesis and Stiff-Man Syndrome, peripheral nervous system diseases such as acrodynia. amyloid neuropathies, autonomic nervous system diseases such as Adie's Syndrome, Barre-Lieou Syndrome, Familial Dysautonomia, Horner's Syndrome, Reflex Sympathetic Dystrophy and Shy-Drager Syndrome, Cranial Nerve Diseases such as Acoustic Nerve Diseases such as Acoustic Neuroma which includes Neurofibromatosis 2, Facial Nerve Diseases such as Facial Neuralgia, Melkersson-Rosenthal Syndrome, ocular motility disorders which includes amblyopia, nystagmus, oculomotor nerve paralysis, ophthalmoplegia such as Duane's Syndrome, Horner's Syndrome, Chronic Progressive External Ophthalmoplegia which includes Kearns Syndrome, Strabismus such as Esotropia and Exotropia, Oculomotor Nerve Paralysis, Optic Nerve Diseases such as Optic Atrophy which includes Hereditary Optic Atrophy, Optic Disk Drusen, Optic Neuritis such as Neuromyelitis Optica, Papilledema, Trigeminal Neuralgia, Vocal Cord Paralysis, Demyelinating Diseases such as Neuromyelitis Optica and Swayback, Diabetic neuropathies such as diabetic foot, nerve compression syndromes such as carpal tunnel syndrome, tarsal tunnel syndrome, thoracic outlet syndrome such as cervical rib syndrome, ulnar nerve compression syndrome, neuralgia such as causalgia, cervico-brachial neuralgia, facial neuralgia and trigeminal neuralgia, neuritis such as experimental allergic neuritis, optic neuritis, polyneuritis, polyradiculoneuritis and radiculities such as polyradiculitis, hereditary motor and sensory neuropathies such as Charcot-Marie Disease, Hereditary Optic Atrophy, Refsum's Disease, Hereditary Spastic Paraplegia and Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies which include Congenital Analgesia and Familial Dysautonomia, POEMS Syndrome, Sciatica, Gustatory Sweating and Tetany).

Infectious Disease

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Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

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Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention. Examples of viruses, include, but are not limited to Examples of viruses, include, but are not limited to the following DNA and RNA viruses and viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Dengue, EBV, HIV, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as. Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza A, Influenza B, and parainfluenza), Papiloma virus, Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, respiratory syncytial virus, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), Japanese B encephalitis, Junin, Chikungunya, Rift Valley fever, yellow fever, meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific

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embodiments, polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat: meningitis, Dengue, EBV, and/or hepatitis (e.g., hepatitis B). In an additional specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat patients nonresponsive to one or more other commercially available hepatitis vaccines. In a further specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat AIDS.

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Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, include, but not limited to, the following Gram-Negative and Gram-positive bacteria and bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Cryptococcus neoformans, Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia (e.g., Borrelia burgdorferi, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, E. coli (e.g., Enterotoxigenic E. coli and Enterohemorrhagic E. coli), Enterobacteriaceae (Klebsiella, Salmonella (e.g., Salmonella typhi, and Salmonella paratyphi), Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Mycobacterium leprae, Vibrio cholerae, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Menigococcal), Meisseria meningitidis, Pasteurellacea Infections (e.g., Actinobacillus, Heamophilus (e.g., Heamophilus influenza type B), Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, Shigella spp., Staphylococcal, Meningiococcal, Pneumococcal and Streptococcal (e.g., Streptococcus pneumoniae and Group B Streptococcus). These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease. respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning,

Typhoid, pneumonia, Gonorrhea, meningitis (e.g., mengitis types A and B), Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, Ppolynucleotides, polypeptides, agonists or antagonists of the invention are used to treat: tetanus, Diptheria, botulism, and/or meningitis type B.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, the following families or class: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas and Sporozoans (e.g., Plasmodium virax, Plasmodium falciparium, Plasmodium malariae and Plasmodium ovale). These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), malaria, pregnancy complications, and toxoplasmosis. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

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Regeneration

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Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteocarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vasculature (including vascular and lymphatics), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stoke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases

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(e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotides or polypeptides, as well as agonists or antagonists of the present invention.

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Chemotaxis

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may have chemotaxis activity. A chemotaxic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may increase chemotaxic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotaxic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could be used as an inhibitor of chemotaxis.

Binding Activity

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit

(antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

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Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide. Preferred cells include cells from mammals, yeast, Drosophila, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

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Additionally, the receptor to which the polypeptide of the present invention binds can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting (Coligan, et al., Current Protocols in Immun., 1(2), Chapter 5, (1991)). For example, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the polypeptides, for example, NIH3T3 cells which are known to contain multiple receptors for the FGF family proteins, and SC-3 cells, and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the polypeptides. Transfected cells which are grown on glass slides are exposed to the polypeptide of the present invention, after they have been labelled. The polypeptides can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase.

Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an iterative sub-pooling and re-screening process, eventually yielding a single clones that encodes the putative receptor.

As an alternative approach for receptor identification, the labeled polypeptides can be photoaffinity linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE analysis and exposed to X-ray film. The labeled complex containing the receptors of the polypeptides can be excised, resolved into peptide fragments, and subjected to protein microsequencing. The amino acid sequence obtained from microsequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the genes encoding the putative receptors.

Moreover, the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling") may be employed to modulate the activities of the polypeptide of the present invention thereby effectively generating agonists and antagonists of the polypeptide of the present invention. See generally, U.S. Patent Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458, and Patten, P. A., et al., Curr. Opinion Biotechnol. 8:724-

33 (1997); Harayama, S. Trends Biotechnol. 16(2):76-82 (1998); Hansson, L. O., et. al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo, M. M. and Blasco, R. Biotechniques 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference). In one embodiment, alteration of polynucleotides and corresponding polypeptides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments into a desired molecule by homologous, or site-specific, recombination. In another embodiment, polynucleotides and corresponding polypeptides may be alterred by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of the polypeptide of the present invention may be recombined with one or more components, motifs, sections, parts, domains. fragments, etc. of one or more heterologous molecules. In preferred embodiments, the heterologous molecules are family members. In further preferred embodiments, the heterologous molecule is a growth factor such as, for example, platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I), transforming growth factor (TGF)-alpha, epidermal growth factor (EGF), fibroblast growth factor (FGF), TGFbeta, bone morphogenetic protein (BMP)-2, BMP-4, BMP-5, BMP-6, BMP-7, activins A and B, decapentaplegic(dpp), 60A, OP-2, dorsalin, growth differentiation factors (GDFs), nodal, MIS, inhibin-alpha, TGF-beta1, TGF-beta2, TGF-beta3, TGFbeta5, and glial-derived neurotrophic factor (GDNF).

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Other preferred fragments are biologically active fragments of the polypeptide of the present invention. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Additionally, this invention provides a method of screening compounds to identify those which modulate the action of the polypeptide of the present invention. An example of such an assay comprises combining a mammalian fibroblast cell, a the polypeptide of the present invention, the compound to be screened and ³[H]

thymidine under cell culture conditions where the fibroblast cell would normally proliferate. A control assay may be performed in the absence of the compound to be screened and compared to the amount of fibroblast proliferation in the presence of the compound to determine if the compound stimulates proliferation by determining the uptake of ³[H] thymidine in each case. The amount of fibroblast cell proliferation is measured by liquid scintillation chromatography which measures the incorporation of ³[H] thymidine. Both agonist and antagonist compounds may be identified by this procedure.

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In another method, a mammalian cell or membrane preparation expressing a receptor for a polypeptide of the present invention is incubated with a labeled polypeptide of the present invention in the presence of the compound. The ability of the compound to enhance or block this interaction could then be measured. Alternatively, the response of a known second messenger system following interaction of a compound to be screened and the receptor is measured and the ability of the compound to bind to the receptor and elicit a second messenger response is measured to determine if the compound is a potential agonist or antagonist. Such second messenger systems include but are not limited to, cAMP guanylate cyclase, ion channels or phosphoinositide hydrolysis.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptides of the invention from suitably manipulated cells or tissues.

Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the present invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the present invention, (b) assaying a biological

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activity, and (b) determining if a biological activity of the polypeptide has been altered.

Targeted Delivery

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In another embodiment, the invention provides a method of delivering compositions to targeted cells expressing a receptor for a polypeptide of the invention, or cells expressing a cell bound form of a polypeptide of the invention.

As discussed herein, polypeptides or antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (including antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention (e.g., polypeptides of the invention or antibodies of the invention) in association with toxins or cytotoxic prodrugs.

By "toxin" is meant compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNAse, alpha

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toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. By "cytotoxic prodrug" is meant a non-toxic compound that is converted by an enzyme, normally present in the cell, into a cytotoxic compound. Cytotoxic prodrugs that may be used according to the methods of the invention include, but are not limited to, glutamyl derivatives of benzoic acid mustard alkylating agent, phosphate derivatives of etoposide or mitomycin C, cytosine arabinoside, daunorubisin, and phenoxyacetamide derivatives of doxorubicin.

10 Drug Screening

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Further contemplated is the use of the polypeptides of the present invention, or the polynucleotides encoding these polypeptides, to screen for molecules which modify the activities of the polypeptides of the present invention. Such a method would include contacting the polypeptide of the present invention with a selected compound(s) suspected of having antagonist or agonist activity, and assaying the activity of these polypeptides following binding.

This invention is particularly useful for screening therapeutic compounds by using the polypeptides of the present invention, or binding fragments thereof, in any of a variety of drug screening techniques. The polypeptide or fragment employed in such a test may be affixed to a solid support, expressed on a cell surface, free in solution, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. One may measure, for example, the formulation of complexes between the agent being tested and a polypeptide of the present invention.

Thus, the present invention provides methods of screening for drugs or any other agents which affect activities mediated by the polypeptides of the present invention. These methods comprise contacting such an agent with a polypeptide of the present invention or a fragment thereof and assaying for the presence of a

complex between the agent and the polypeptide or a fragment thereof, by methods well known in the art. In such a competitive binding assay, the agents to screen are typically labeled. Following incubation, free agent is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of a particular agent to bind to the polypeptides of the present invention.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the polypeptides of the present invention, and is described in great detail in European Patent Application 84/03564, published on September 13, 1984, which is incorporated herein by reference herein. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with polypeptides of the present invention and washed. Bound polypeptides are then detected by methods well known in the art. Purified polypeptides are coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies may be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding polypeptides of the present invention specifically compete with a test compound for binding to the polypeptides or fragments thereof. In this manner, the antibodies are used to detect the presence of any peptide which shares one or more antigenic epitopes with a polypeptide of the invention.

Antisense And Ribozyme (Antagonists)

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In specific embodiments, antagonists according to the present invention are nucleic acids corresponding to the sequences contained in SEQ ID NO:X, or the complementary strand thereof, and/or to nucleotide sequences contained in the cDNA contained in the related cDNA clone identified in Table 1. In one embodiment, antisense sequence is generated internally, by the organism, in another embodiment, the antisense sequence is separately administered (see, for example, O'Connor, J.,

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Neurochem. 56:560 (1991). Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Antisense technology can be used to control gene expression through antisense DNA or RNA, or through triple-helix formation. Antisense techniques are discussed for example, in Okano, J., Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance, Lee et al., Nucleic Acids Research 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1300 (1991). The methods are based on binding of a polynucleotide to a complementary DNA or RNA.

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For example, the use of c-myc and c-myb antisense RNA constructs to inhibit the growth of the non-lymphocytic leukemia cell line HL-60 and other cell lines was previously described. (Wickstrom et al. (1988); Anfossi et al. (1989)). These experiments were performed in vitro by incubating cells with the oligoribonucleotide. A similar procedure for in vivo use is described in WO 91/15580. Briefly, a pair of oligonucleotides for a given antisense RNA is produced as follows: A sequence complimentary to the first 15 bases of the open reading frame is flanked by an EcoR1 site on the 5 end and a HindIII site on the 3 end. Next, the pair of oligonucleotides is heated at 90°C for one minute and then annealed in 2X ligation buffer (20mM TRIS HCl pH 7.5, 10mM MgCl2, 10MM dithiothreitol (DTT) and 0.2 mM ATP) and then ligated to the EcoR1/Hind III site of the retroviral vector PMV7 (WO 91/15580).

For example, the 5' coding portion of a polynucleotide that encodes the polypeptide of the present invention may be used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription thereby preventing transcription and the production of the receptor. The antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into receptor polypeptide.

In one embodiment, the antisense nucleic acid of the invention is produced intracellularly by transcription from an exogenous sequence. For example, a vector or a portion thereof, is transcribed, producing an antisense nucleic acid (RNA) of the

invention. Such a vector would contain a sequence encoding the antisense nucleic acid. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art, used for replication and expression in vertebrate cells. Expression of the sequence encoding the polypeptide of the present invnetion or fragments thereof, can be by any promoter known in the art to act in vertebrate, preferably human cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, Nature 29:304-310 (1981), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., Cell 22:787-797 (1980), the herpes thymidine promoter (Wagner et al., Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445 (1981), the regulatory sequences of the metallothionein gene (Brinster, et al., Nature 296:39-42 (1982)), etc.

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The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a gene of the present invention. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the larger the hybridizing nucleic acid, the more base mismatches with a RNA it may contain and still form a stable duplex (or triplex as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

Oligonucleotides that are complementary to the 5' end of the message, e.g., the 5' untranslated sequence up to and including the AUG initiation codon, should work most efficiently at inhibiting translation. However, sequences complementary to the

3' untranslated sequences of mRNAs have been shown to be effective at inhibiting translation of mRNAs as well. See generally, Wagner, R., 1994, Nature 372:333-335. Thus, oligonucleotides complementary to either the 5'- or 3'- non- translated, non-coding regions of polynucleotide sequences described herein could be used in an antisense approach to inhibit translation of endogenous mRNA. Oligonucleotides complementary to the 5' untranslated region of the mRNA should include the complement of the AUG start codon. Antisense oligonucleotides complementary to mRNA coding regions are less efficient inhibitors of translation but could be used in accordance with the invention. Whether designed to hybridize to the 5'-, 3'- or coding region of mRNA of the present invention, antisense nucleic acids should be at least six nucleotides in length, and are preferably oligonucleotides ranging from 6 to about 50 nucleotides in length. In specific aspects the oligonucleotide is at least 10 nucleotides, at least 17 nucleotides, at least 25 nucleotides or at least 50 nucleotides.

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The polynucleotides of the invention can be DNA or RNA or chimeric mixtures or derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone, for example, to improve stability of the molecule, hybridization, etc. The oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors in vivo), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. U.S.A. 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. 84:648-652; PCT Publication No. WO88/09810, published December 15, 1988) or the blood-brain barrier (see, e.g., PCT Publication No. WO89/10134, published April 25, 1988), hybridization-triggered cleavage agents. (See, e.g., Krol et al., 1988, BioTechniques 6:958-976) or intercalating agents. (See, e.g., Zon, 1988, Pharm. Res. 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The antisense oligonucleotide may comprise at least one modified base moiety which is selected from the group including, but not limited to, 5-fluorouracil,

5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, inosine. 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine. 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil. 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

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The antisense oligonucleotide may also comprise at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the antisense oligonucleotide comprises at least one modified phosphate backbone selected from the group including, but not limited to, a phosphorothioate, a phosphorodithioate, a phosphoramidate, a phosphoramidate, a phosphoramidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal or analog thereof.

In yet another embodiment, the antisense oligonucleotide is an a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual b-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641). The oligonucleotide is a 2'-0-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330).

Polynucleotides of the invention may be synthesized by standard methods 30 known in the art, e.g. by use of an automated DNA synthesizer (such as are

commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451), etc.

While antisense nucleotides complementary to the coding region sequence could be used, those complementary to the transcribed untranslated region are most preferred.

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Potential antagonists according to the invention also include catalytic RNA, or a ribozyme (See, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al, Science 247:1222-1225 (1990). While ribozymes that cleave mRNA at site specific recognition sequences can be used to destroy mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'. The construction and production of hammerhead ribozymes is well known in the art and is described more fully in Haseloff and Gerlach, Nature 334:585-591 (1988). There are numerous potential hammerhead ribozyme cleavage sites within the nucleotide sequence of SEQ ID NO:X. Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the mRNA; i.e., to increase efficiency and minimize the intracellular accumulation of non-functional mRNA transcripts.

As in the antisense approach, the ribozymes of the invention can be composed of modified oligonucleotides (e.g. for improved stability, targeting, etc.) and should be delivered to cells which express in vivo. DNA constructs encoding the ribozyme may be introduced into the cell in the same manner as described above for the introduction of antisense encoding DNA. A preferred method of delivery involves using a DNA construct "encoding" the ribozyme under the control of a strong constitutive promoter, such as, for example, pol III or pol II promoter, so that transfected cells will produce sufficient quantities of the ribozyme to destroy

endogenous messages and inhibit translation. Since ribozymes unlike antisense molecules, are catalytic, a lower intracellular concentration is required for efficiency.

Antagonist/agonist compounds may be employed to inhibit the cell growth and proliferation effects of the polypeptides of the present invention on neoplastic cells and tissues, i.e. stimulation of angiogenesis of tumors, and, therefore, retard or prevent abnormal cellular growth and proliferation, for example, in tumor formation or growth.

The antagonist/agonist may also be employed to prevent hyper-vascular diseases, and prevent the proliferation of epithelial lens cells after extracapsular cataract surgery. Prevention of the mitogenic activity of the polypeptides of the present invention may also be desirous in cases such as restenosis after balloon angioplasty.

The antagonist/agonist may also be employed to prevent the growth of scar tissue during wound healing.

The antagonist/agonist may also be employed to treat the diseases described herein.

Thus, the invention provides a method of treating disorders or diseases, including but not limited to the disorders or diseases listed throughout this application, associated with overexpression of a polynucleotide of the present invention by administering to a patient (a) an antisense molecule directed to the polynucleotide of the present invention, and/or (b) a ribozyme directed to the polynucleotide of the present invention.

Other Activities

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A polypeptide, polynucleotide, agonist, or antagonist of the present invention, as a result of the ability to stimulate vascular endothelial cell growth, may be employed in treatment for stimulating re-vascularization of ischemic tissues due to various disease conditions such as thrombosis, arteriosclerosis, and other cardiovascular conditions. The polypeptide, polynucleotide, agonist, or antagonist of

the present invention may also be employed to stimulate angiogenesis and limb regeneration, as discussed above.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for treating wounds due to injuries, burns, post-operative tissue repair, and ulcers since they are mitogenic to various cells of different origins, such as fibroblast cells and skeletal muscle cells, and therefore, facilitate the repair or replacement of damaged or diseased tissue.

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A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed stimulate neuronal growth and to treat and prevent neuronal damage which occurs in certain neuronal disorders or neuro-degenerative conditions such as Alzheimer's disease, Parkinson's disease, and AIDS-related complex. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may have the ability to stimulate chondrocyte growth, therefore, they may be employed to enhance bone and periodontal regeneration and aid in tissue transplants or bone grafts.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be also be employed to prevent skin aging due to sunburn by stimulating keratinocyte growth.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for preventing hair loss, since FGF family members activate hair-forming cells and promotes melanocyte growth. Along the same lines, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be employed to stimulate growth and differentiation of hematopoietic cells and bone marrow cells when used in combination with other cytokines.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to maintain organs before transplantation or for supporting cell culture of primary tissues. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for inducing tissue of mesodermal origin to differentiate in early embryos.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, caricadic rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

The above-recited applications have uses in a wide variety of hosts. Such hosts include, but are not limited to, human, murine, rabbit, goat, guinea pig, camel, horse, mouse, rat, hamster, pig, micro-pig, chicken, goat, cow, sheep, dog, cat, non-human primate, and human. In specific embodiments, the host is a mouse, rabbit, goat, guinea pig, chicken, rat, hamster, pig, sheep, dog or cat. In preferred embodiments, the host is a mammal. In most preferred embodiments, the host is a human.

Other Preferred Embodiments

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Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

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Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in

the related cDNA clone contained in the deposit, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises a cDNA clone contained in the deposit.

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Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of an open reading frame sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the

complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

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Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleotide sequence of SEQ ID NO:X; or the cDNA in the related cDNA clone identified in Table 1 which encodes a protein, wherein the method comprises a step of detecting in a biological sample

obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence of the cDNA in the related cDNA clone contained in the deposit.

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Also preferred is the above method for diagnosing a pathological condition which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a DNA microarray or "chip" of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, 100, 150, 200, 250, 300, 500, 1000, 2000, 3000 or 4000 nucleotide sequences, wherein at least one sequence in said DNA microarray or "chip" is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the cDNA clone referenced in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the

polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

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Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a portion of said polypeptide encoded by the cDNA clone referenced in Table 1; a polypeptide encoded by SEQ ID NO:X; and/or the polypeptide sequence of SEQ ID NO:Y.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

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Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X;

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and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

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Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleic acid sequence identified in Table 1 encoding a polypeptide, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

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Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a human protein comprising an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a protein activity, which method comprises administering to such

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an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to increase the level of said protein activity in said individual.

Also preferred is a method of treatment of an individual in need of a decreased level of a protein activity, which method comprised administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to decrease the level of said protein activity in said individual.

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Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

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Examples

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Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

Each deposited cDNA clone is contained in a plasmid vector. Table 5 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The following correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 5 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	Vector Used to Construct Library	Corresponding Deposited Plasmid
	Lambda Zap	pBluescript (pBS)
	Uni-Zap XR	pBluescript (pBS)
15	Zap Express	pBK
	lafmid BA	plafmid BA
	pSport1	pSport1
	pCMVSport 2.0	pCMVSport 2.0
	pCMVSport 3.0	pCMVSport 3.0
20	pCR [®] 2.1	pCR [®] 2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3

primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the fl origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the fl ori generates sense strand DNA and in the other, antisense.

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Vectors pSport1, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 5, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited by reference to Table 2 and 5 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone referenced in Table 1.

TABLE 5

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HUKA HUKB HUKC HUKD HUKE HUKF HUKG	Human Uterine Cancer	Lambda ZAP II	LP01
HCNA HCNB	Human Colon	Lambda Zap II	LP01
HFFA	Human Fetal Brain, random primed	Lambda Zap II	LP01
HTWA	Resting T-Cell	Lambda ZAP II	LP01
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP01
HLMB HLMF HLMG HLMH HLMI HLMJ HLMM HLMN	breast lymph node CDNA library	Lambda ZAP II	LP01
HCQA HCQB	human colon cancer	Lamda ZAP II	LP01
HMEA HMEC HMED HMEE HMEF HMEG HMEI HMEJ HMEK HMEL	Human Microvascular Endothelial Cells, fract. A	Lambda ZAP II	LPOI
HUSA HUSC	Human Umbilical Vein Endothelial Cells, fract. A	Lambda ZAP II	LP01
HLQA HLQB	Hepatocellular Tumor	Lambda ZAP II	LP01
HHGA HHGB HHGC HHGD	Hemangiopericytoma	Lambda ZAP II	LP01
HSDM	Human Striatum Depression, re-rescue	Lambda ZAP II	LP01
HUSH	H Umbilical Vein Endothelial Cells, frac A, re-excision	Lambda ZAP II	LP01
HSGS	Salivary gland, subtracted	Lambda ZAP II	LP01
HFXA HFXB HFXC HFXD HFXE HFXF HFXG HFXH	Brain frontal cortex	Lambda ZAP II	LP01
НРОЛ НРОВ НРОС	PERM TF274	Lambda ZAP II	LP01
HFXJ HFXK	Brain Frontal Cortex, re-excision	Lambda ZAP II	LP01
HCWA HCWB HCWC HCWD HCWE HCWF HCWG HCWH HCWI HCWJ HCWK	CD34 positive cells (Cord Blood)	ZAP Express	LP02
HCUA HCUB HCUC	CD34 depleted Buffy Coat (Cord Blood)	ZAP Express	LP02
HRSM	A-14 cell line	ZAP Express	LP02
HRSA	A1-CELL LINE	ZAP Express	LP02
HCUD HCUE HCUF HCUG HCUH HCUI	CD34 depleted Buffy Coat (Cord Blood), re-excision	ZAP Express	LP02
HBXE HBXF HBXG	H. Whole Brain #2, re-excision	ZAP Express	LP02
HRLM	L8 cell line	ZAP Express	LP02
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP02
HUDA HUDB HUDC	Testes	ZAP Express	LP02
ннтм ннто	H. hypothalamus, frac A;re-excision	ZAP Express	LP02
HHTL	H. hypothalamus, frac A	ZAP Express	LP02
HASA HASD	Human Adult Spicen	Uni-ZAP XR	LP03
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP03
HE8A HE8B HE8C HE8D HE8E HE8F HE8M HE8N	Human 8 Week Whole Embryo	Uni-ZAP XR	LP03
HGBA HGBD HGBE HGBF HGBG HGBH HGBI	Human Gall Bladder	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HLHA HLHB HLHC HLHD HLHE HLHF HLHG HLHH HLHQ	Human Fetal Lung III	Uni-ZAP XR	LP03
НРМА НРМВ НРМС НРМО НРМЕ НРМГ НРМG НРМН	Human Placenta	Uni-ZAP XR	LP03
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP03
HSIA HSIC HSID HSIE	Human Adult Small Intestine	Uni-ZAP XR	LP03
HTEA HTEB HTEC HTED HTEE HTEF HTEG HTEH HTEI HTEJ HTEK	Human Testes	Uni-ZAP XR	LP03
HTPA HTPB HTPC HTPD HTPE	Human Pancreas Tumor	Uni-ZAP XR	LP03
HTTA HTTB HTTC HTTD HTTE HTTF	Human Testes Tumor	Uni-ZAP XR	LP03
НАРА НАРВ НАРС НАРМ	Human Adult Pulmonary	Uni-ZAP XR	LP03
HETA HETB HETC HETD HETE HETF HETG HETH HETI	Human Endometrial Tumor	Uni-ZAP XR	LP03
HHFB HHFC HHFD HHFE HHFF HHFG HHFH HHFI	Human Fetal Heart	Uni-ZAP XR	LP03
ННРВ ННРС ННРО ННРЕ ННРГ ННРС ННРН	Human Hippocampus	Uni-ZAP XR	LP03
HCE1 HCE2 HCE3 HCE4 HCE5 HCEB HCEC HCED HCEE HCEF HCEG		Uni-ZAP XR	LP03
HUVB HUVC HUVD HUVE	Human Umbilical Vein, Endo, remake	Uni-ZAP XR	LP03
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP03
HTAA HTAB HTAC HTAD HTAE	Human Activated T-Cells	Uni-ZAP XR	LP03
HFEA HFEB HFEC	Human Fetal Epithelium (Skin)	Uni-ZAP XR	LP03
НЈРА НЈРВ НЈРС НЈРD	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Uni-ZAP XR	LP03
HESA	Human epithelioid sarcoma	Uni-Zap XR	LP03
HLTA HLTB HLTC HLTD HLTE HLTF	Human T-Cell Lymphoma	Uni-ZAP XR	LP03
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP03
HRDA HRDB HRDC HRDD HRDE HRDF	Human Rhabdomyosarcoma	Uni-ZAP XR	LP03
HCAA HCAB HCAC	Cem cells cyclohexamide treated	Uni-ZAP XR	LP03
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HSUA HSUB HSUC HSUM	Supt Cells, cyclohexamide treated	Uni-ZAP XR	LP03
HT4A HT4C HT4D	Activated T-Cells, 12 hrs.	Uni-ZAP XR	LP03
HE9A HE9B HE9C HE9D HE9E HE9F HE9G HE9H HE9M HE9N	Nine Week Old Early Stage Human	Uni-ZAP XR	LP03
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP03
HTSA	Activated T-Cells, 24 hrs.	Uni-ZAP XR	LP03
HFGA HFGM	Human Fetal Brain	Uni-ZAP XR	LP03
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP03
HBGB HBGD	Human Primary Breast Cancer	Uni-ZAP XR	LP03
HBNA HBNB	Human Normal Breast	Uni-ZAP XR	LP03
HCAS	Cem Cells, cyclohexamide treated, subtra	Uni-ZAP XR	LP03
HHPS	Human Hippocampus, subtracted	pBS	LP03
HKCS HKCU	Human Colon Cancer, subtracted	pBS	LP03
HRGS	Raji cells, cyclohexamide treated,	pBS	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	subtracted		
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBS	LP03
HT4S	Activated T-Cells, 12 hrs, subtracted	Uni-ZAP XR	LP03
HCDA HCDB HCDC HCDD HCDE	Human Chondrosarcoma	Uni-ZAP XR	LP03
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP03
HTLA HTLB HTLC HTLD HTLE HTLF	Human adult testis, large inserts	Uni-ZAP XR	LP03
HLMA HLMC HLMD	Breast Lymph node cDNA library	Uni-ZAP XR	LP03
H6EA H6EB H6EC	HL-60, PMA 4H	Uni-ZAP XR	LP03
HTXA HTXB HTXC HTXD HTXE HTXF HTXG HTXH	Activated T-Cell (12hs)/Thiouridine labelledEco	Uni-ZAP XR	LP03
HNFA HNFB HNFC HNFD HNFE HNFF HNFG HNFH HNFJ	Human Neutrophil, Activated	Uni-ZAP XR	LP03
НТОВ НТОС	HUMAN TONSILS, FRACTION 2	Uni-ZAP XR	LP03
НМСВ	Human OB MG63 control fraction I	Uni-ZAP XR	LP03
НОРВ	Human OB HOS control fraction I	Uni-ZAP XR	LP03
HORB	Human OB HOS treated (10 nM E2) fraction I	Uni-ZAP XR	LP03
HSVA HSVB HSVC	Human Chronic Synovitis	Uni-ZAP XR	LP03
HROA	HUMAN STOMACH	Uni-ZAP XR	LP03
НВЈА НВЈВ НВЈС НВЈО НВЈЕ НВЈҒ НВЈС НВЈН НВЈІ НВЈЈ НВЈК	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP03
HCRA HCRB HCRC	human corpus colosum	Uni-ZAP XR	LP03
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP03
HDSA	Dermatofibrosarcoma Protuberance	Uni-ZAP XR	LP03
HMWA HMWB HMWC HMWD HMWE HMWF HMWG HMWH HMWI HMWJ	Bone Marrow Cell Line (RS4;11)	Uni-ZAP XR	LP03
ASOA	stomach cancer (human)	Uni-ZAP XR	LP03
HERA	SKIN	Uni-ZAP XR	LP03
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP03
IGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP03
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP03
НВСА НВСВ	H. Lymph node breast Cancer	Uni-ZAP XR	LP03
IPWT	Human Prostate BPH, re-excision	Uni-ZAP XR	LP03
HFVG HFVH HFVI	Fetal Liver, subtraction II	pBS	LP03
INFI	Human Neutrophils, Activated, re-	pBS	LP03
НВМВ НВМС НВМD	Human Bone Marrow, re-excision	pBS	LP03
НКМІ НКММ НКММ	H. Kidney Medulla, re-excision	pBS	LP03
IKIX HKIY	H. Kidney Cortex, subtracted	pBS	LP03
ADT	H. Amygdala Depression, subtracted	pBS	LP03
16AS	HI-60, untreated, subtracted	Uni-ZAP XR	LP03
16ES	HL-60, PMA 4H, subtracted	Uni-ZAP XR	LP03
16BS	HL-60, RA 4h, Subtracted	Uni-ZAP XR	LP03
16CS	HL-60, PMA 1d, subtracted	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
НТХЈ НТХК	Activated T-cell(12h)/Thiouridine-re-	Uni-ZAP XR	LP03
HMSA HMSB HMSC HMSD HMSE HMSF HMSG HMSH HMSI HMSJ HMSK	Monocyte activated	Uni-ZAP XR	LP03
HAGA HAGB HAGC HAGD HAGE HAGF	Human Amygdala	Uni-ZAP XR	LP03
HSRA HSRB HSRE	STROMAL -OSTEOCLASTOMA	Uni-ZAP XR	LP03
HSRD HSRF HSRG HSRH	Human Osteoclastoma Stromal Cells - unamplified	Uni-ZAP XR	LP03
HSQA HSQB HSQC HSQD HSQE HSQF HSQG	Stromal cell TF274	Uni-ZAP XR	LP03
HSKA HSKB HSKC HSKD HSKE HSKF HSKZ	Smooth muscle, serum treated	Uni-ZAP XR	LP03
HSLA HSLB HSLC HSLD HSLE HSLF HSLG	Smooth muscle.control	Uni-ZAP XR	LP03
HSDA HSDD HSDE HSDF HSDG HSDH	Spinal cord	Uni-ZAP XR	LP03
HPWS	Prostate-BPH subtracted II	pBS	LP03
HSKW HSKX HSKY	Smooth Muscle- HASTE normalized	pBS	LP03
HFPB HFPC HFPD	H. Frontal cortex.epileptic;re-excision	Uni-ZAP XR	LP03
HSDI HSDJ HSDK	Spinal Cord, re-excision	Uni-ZAP XR	LP03
HSKN HSKO	Smooth Muscle Serum Treated, Norm	pBS	LP03
HSKG HSKH HSKI	Smooth muscle, serum induced,re-exc	pBS	LP03
HFCA HFCB HFCC HFCD HFCE HFCF	Human Fetal Brain	Uni-ZAP XR	LP04
HPTA HPTB HPTD	Human Pituitary	Uni-ZAP XR	LP04
НТНВ HTHC HTHD	Human Thymus	Uni-ZAP XR	LP04
HE6B HE6C HE6D HE6E HE6F HE6G HE6S	Human Whole Six Week Old Embryo	Uni-ZAP XR	LP04
HSSA HSSB HSSC HSSD HSSE HSSF HSSG HSSH HSSI HSSJ HSSK	Human Synovial Sarcoma	Uni-ZAP XR	LP04
HE7T	7 Week Old Early Stage Human, subtracted	Uni-ZAP XR	LP04
НЕРА НЕРВ НЕРС	Human Epididymus	Uni-ZAP XR	LP04
HSNA HSNB HSNC HSNM HSNN	Human Synovium	Uni-ZAP XR	LP04
HPFB HPFC HPFD HPFE	Human Prostate Cancer, Stage C fraction	Uni-ZAP XR	LP04
HE2A HE2D HE2E HE2H HE2I HE2M HE2N HE2O		Uni-ZAP XR	LP04
HE2B HE2C HE2F HE2G HE2P HE2Q		Uni-ZAP XR	LP04
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP04
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP04
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP04
HWTA HWTB HWTC	wilm's tumor	Uni-ZAP XR	LP04
HBSD	Bone Cancer, re-excision	Uni-ZAP XR	LP04
HSGB	Salivary gland, re-excision	Uni-ZAP XR	LP04
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP04
HSXA HSXB HSXC HSXD	Human Substantia Nigra	Uni-ZAP XR	LP04
НЅНА НЅНВ НЅНС	Smooth muscle, IL1b induced	Uni-ZAP XR	LP04

Libraries owned by Catalog	Catalog Description	Vector	ATCC
HOUA HOUB HOUC HOUD HOUE	Adipocytes	Uni-ZAP XR	Deposit LP04
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	
HELA HELB HELC HELD HELE	Endothelial cells-control	Uni-ZAP XR	LP04
HELF HELG HELH			LP04
HEMA HEMB HEMC HEMD HEME HEMF HEMG HEMH	Endothelial-induced	Uni-ZAP XR	LP04
НВІА НВІВ НВІС	Human Brain, Striatum	Uni-ZAP XR	LP04
HHSA HHSB HHSC HHSD HHSE	Human Hypothalmus.Schizophrenia	Uni-ZAP XR	LP04
HNGA HNGB HNGC HNGD HNGE HNGF HNGG HNGH HNGI HNGJ	neutrophils control	Uni-ZAP XR	LP04
HNHA HNHB HNHC HNHD HNHE HNHF HNHG HNHH HNHI HNHJ	Neutrophils IL-1 and LPS induced	Uni-ZAP XR	LP04
HSDB HSDC	STRIATUM DEPRESSION	Uni-ZAP XR	LP04
ННРТ	Hypothalamus	Uni-ZAP XR	LP04
HSAT HSAU HSAV HSAW HSAX HSAY HSAZ	Anergic T-cell	Uni-ZAP XR	LP04
НВМЅ НВМТ НВМИ НВМ∨ НВМW НВМХ	Bone marrow	Uni-ZAP XR	LP04
HOEA HOEB HOEC HOED HOEE HOEF HOEJ	Osteoblasts	Uni-ZAP XR	LP04
HAIA HAIB HAIC HAID HAIE HAIF	Epithelial-TNFa and INF induced	Uni-ZAP XR	LP04
HTGA HTGB HTGC HTGD	Apoptotic T-cell	Uni-ZAP XR	LP04
HMCA HMCB HMCC HMCD HMCE	Macrophage-oxLDL	Uni-ZAP XR	LP04
HMAA HMAB HMAC HMAD HMAE HMAF HMAG	Macrophage (GM-CSF treated)	Uni-ZAP XR	LP04
НРНА	Normal Prostate	Uni-ZAP XR	LP04
НРІА НРІВ НРІС	LNCAP prostate cell line	Uni-ZAP XR	LP04
НРЈА НРЈВ НРЈС	PC3 Prostate cell line	Uni-ZAP XR	LP04
HOSE HOSF HOSG	Human Osteoclastoma, re-excision	Uni-ZAP XR	LP04
HTGE HTGF	Apoptotic T-cell, re-excision	Uni-ZAP XR	LP04
HMAJ HMAK	H Macrophage (GM-CSF treated), re-	Uni-ZAP XR	LP04
HACB HACC HACD	Human Adipose Tissue, re-excision	Uni-ZAP XR	LP04
HFPA	H. Frontal Cortex, Epileptic	Uni-ZAP XR	LP04
HFAA HFAB HFAC HFAD HFAE	Alzheimers, spongy change	Uni-ZAP XR	LP04
HFAM	Frontal Lobe, Dementia	Uni-ZAP XR	LP04
НМІА НМІВ НМІС	Human Manic Depression Tissue	Uni-ZAP XR	LP04
HTSA HTSE HTSF HTSG HTSH	Human Thymus	pBS	LP05
НРВА НРВВ НРВС НРВО НРВЕ	Human Pineal Gland	pBS	LP05
HSAA HSAB HSAC	HSA 172 Cells	pBS	LP05
HSBA HSBB HSBC HSBM	HSC172 cells	pBS	LP05
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBS	LP05
НЈВА НЈВВ НЈВС НЈВD	Jurkat T-Cell, S phase	pBS	LP05
НАГА НАГВ	Aorta endothelial cells + TNF-a	pBS	LP05
HAWA HAWB HAWC	Human White Adipose	pBS	LP05
HTNA HTNB	Human Thyroid	pBS	LP05
HONA	Normal Ovary, Premenopausal	pBS	LP05

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HARA HARB	Human Adult Retina	pBS	LP05
HLJA HLJB	Human Lung	pCMVSport I	LP06
HOFM HOFN HOFO	H. Ovarian Tumor, II, OV5232	pCMVSport 2.0	LP07
HOGA HOGB HOGC	OV 10-3-95	pCMVSport 2.0	LP07
HCGL	CD34+cells. II	pCMVSport 2.0	LP07
HDLA	Hodgkin's Lymphoma I	pCMVSport 2.0	LP07
HDTA HDTB HDTC HDTD HDTE	Hodgkin's Lymphoma II	pCMVSport 2.0	LP07
HKAA HKAB HKAC HKAD HKAE HKAF HKAG HKAH	Keratinocyte	pCMVSport2.0	LP07
НСІМ	CAPFINDER, Crohn's Disease, lib 2	pCMVSport 2.0	LP07
HKAL	Keratinocyte, lib 2	pCMVSport2.0	LP07
HKAT	Keratinocyte, lib 3	pCMVSport2.0	LP07
HNDA	Nasal polyps	pCMVSport2.0	LP07
HDRA	H. Primary Dendritic Cells, lib 3	pCMVSport2.0	LP07
НОНА НОНВ НОНС	Human Osteoblasts II	pCMVSport2.0	LP07
HLDA HLDB HLDC	Liver, Hepatoma	pCMVSport3.0	LP08
HLDN HLDO HLDP	Human Liver, normal	pCMVSport3.0	LP08
НМТА	pBMC stimulated w/ poly I/C	pCMVSport3.0	LP08
HNTA	NTERA2, control	pCMVSport3.0	LP08
HDPA HDPB HDPC HDPD HDPF HDPG HDPH HDPI HDPJ HDPK	Primary Dendritic Cells, lib 1	pCMVSport3.0	LP08
HDPM HDPN HDPO HDPP	Primary Dendritic cells, frac 2	pCMVSport3.0	LP08
HMUA HMUB HMUC	Myoloid Progenitor Cell Line	pCMVSport3.0	LP08
HHEA HHEB HHEC HHED	T Cell helper I	pCMVSport3.0	LP08
ННЕМ ННЕО ННЕР	T cell helper II	pCMVSport3.0	LP08
HEQA HEQB HEQC	Human endometrial stromal cells	pCMVSport3.0	LP08
НЈМА НЈМВ	Human endometrial stromal cells- treated with progesterone	pCMVSport3.0	LP08
HSWA HSWB HSWC	Human endometrial stromal cells- treated with estradiol	pCMVSport3.0	LP08
HSYA HSYB HSYC	Human Thymus Stromal Cells	pCMVSport3.0	LP08
ILWA HLWB HLWC	Human Placenta	pCMVSport3.0	LP08
HRAA HRAB HRAC	Rejected Kidney, lib 4	pCMVSport3.0	LP08
НМТМ	PCR, pBMC I/C treated	PCRII	LP09
НМЈА	H. Meniingima, M6	pSport 1	LP10
HMKA HMKB HMKC HMKD HMKE		pSport 1	LP10
HUSG HUSI	Human umbilical vein endothelial cells, IL-4 induced	pSport 1	LP10
HUSX HUSY	Human Umbilical Vein Endothelial Cells, uninduced	pSport I	LP10
HOFA	Ovarian Tumor I, OV5232	pSport 1	LP10
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport I	LP10
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport 1	LP10
HADA HADC HADD HADE HADF HADG	Human Adipose	pSport 1	LP10
HOVA HOVB HOVC	Human Ovary	pSport 1	LP10

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HTWB HTWC HTWD HTWE HTWF	Resting T-Cell Library,II	pSport I	LP10
НММА	Spleen metastic melanoma	pSport I	LP10
HLYA HLYB HLYC HLYD HLYE	Spleen, Chronic lymphocytic leukemia	pSport I	LP10
HCGA	CD34+ cell, I	pSport I	LPIO
HEOM HEON	Human Eosinophils	pSport I	LP10
HTDA	Human Tonsil, Lib 3	pSport I	LPIO
HSPA	Salivary Gland, Lib 2	pSport I	LP10
НСНА НСНВ НСНС	Breast Cancer cell line, MDA 36	pSport I	LP10
HCHM HCHN	Breast Cancer Cell line, angiogenic	pSport 1	LP10
HCIA	Crohn's Disease	pSport 1	LP10
HDAA HDAB HDAC	HEL cell line	pSport I	LP10
HABA	Human Astrocyte	pSport 1	LP10
HUFA HUFB HUFC	Ulcerative Colitis	pSport 1	LP10
HNTM	NTERA2 + retinoic acid, 14 days	pSport 1	LP10
HDQA	Primary Dendritic cells, CapFinder2, frac 1	pSport I	LP10
HDQM	Primary Dendritic Cells, CapFinder, frac 2	pSport l	LP10
HLDX	Human Liver, normal,CapFinder	pSport 1	LP10
HULA HULB HULC	Human Dermal Endothelial Cells,untreated	pSport1	LP10
НИМА	Human Dermal Endothelial cells,treated	pSportI	LP10
HCJA	Human Stromal Endometrial fibroblasts, untreated	pSport1	LP10
НСЈМ	treated w/ estradiol	pSport1	LP10
HEDA	Human Stromal endometrial fibroblasts, treated with progesterone	pSport1	LP10
HFNA	Human ovary tumor cell OV350721	pSport1	LP10
HKGA HKGB HKGC HKGD	Merkel Cells	pSport1	LP10
HISA HISB HISC	Pancreas Islet Cell Tumor	pSport1	LP10
HLSA	Skin, burned	pSport1	LP10
HBZA	Prostate, BPH, Lib 2	pSport I	LP10
HBZS	Prostate BPH,Lib 2, subtracted	pSport 1	LP10
HFIA HFIB HFIC	Synovial Fibroblasts (control)	pSport 1	LP10
HFIH HFII HFIJ	Synovial hypoxia	pSport 1	LP10
HFIT HFIU HFIV	Synovial IL-1/TNF stimulated	pSport I	LP10
HGCA	Messangial cell, frac 1	pSport1	LP10
HMVA HMVB HMVC	Bone Marrow Stromal Cell, untreated	pSport1	LP10
HFIX HFIY HFIZ	Synovial Fibroblasts (III/TNF), subt	pSport1	LP10
HFOX HFOY HFOZ	Synovial hypoxia-RSF subtracted	pSport1	LP10
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP11
HLIA HLIB HLIC	Human Liver	pCMVSport i	LP012
ННВА ННВВ ННВС ННВD ННВЕ	Human Heart	pCMVSport 1	LP012
НВВА НВВВ	Human Brain	pCMVSport I	LP012
HLJA HLJB HLJC HLJD HLJE	Human Lung	pCMVSport I	LP012

Libraries owned by Catalog	Catalog Description	Vector .	ATCC Deposit
HOGA HOGB HOGC	Ovarian Tumor	pCMVSport 2.0	LP012
MLTH	Human Tonsils. Lib 2	pCMVSport 2.0	LP012
HAMF HAMG	КМН2	pCMVSport 3.0	LP012
НАЈА НАЈВ НАЈС	L428	pCMVSport 3.0	LP012
HWBA HWBB HWBC HWBD HWBE	Dendritic cells, pooled	pCMVSport 3.0	LP012
HWAA HWAB HWAC HWAD HWAE	Human Bone Marrow, treated	pCMVSport 3.0	LP012
НҮАА НҮАВ НҮАС	B Cell lymphoma	pCMVSport 3.0	LP012
нwнg нwнн нwні	Healing groin wound, 6.5 hours post incision	pCMVSport 3.0	LP012
HWHP HWHQ HWHR	Healing groin wound: 7.5 hours post incision	pCMVSport 3.0	LP012
HARM	Healing groin wound - zero hr post- incision (control)	pCMVSport 3.0	LP012
нвім	Olfactory epithelium: nasalcavity	pCMVSport 3.0	LP012
HWDA .	Healing Abdomen wound; 70&90 min post incision	pCMVSport 3.0	LP012
HWEA	Healing Abdomen Wound;15 days post incision	pCMVSport 3.0	LP012
HWJA	Healing Abdomen Wound;21&29 days	pCMVSport 3.0	LP012
HNAL	Human Tongue, frac 2	pSport1	LP012
НМЈА	H. Meniingima, M6	pSport1	LP012
НМКА НМКВ НМКС НМКД НМКЕ	H. Meningima, M1	pSportI	LP012
HOFA	Ovarian Tumor I, OV5232	pSport	LP012
HCFA HCFB HCFC HCFD	T-Cell PHA 16 hrs	pSport1	LP012
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport1	LP012
НММА НММВ НММС	Spleen metastic melanoma	pSport1	LP012
HTDA	Human Tonsil, Lib 3	pSport1	LP012
HDBA	Human Fetal Thymus	pSport1	LP012
HDUA	Pericardium	pSport1	LP012
HBZA	Prostate,BPH, Lib 2	pSport1	LP012
HWCA	Larynx tumor	pSport1	LP012
HWKA	Normal lung	pSport1	LP012
HSMB	Bone marrow stroma,treated	pSport1	LP012
НВНМ	Normal trachea	pSport1	LP012
HLFC	Human Larynx	pSport1	LP012
HLRB	Siebben Polyposis	pSport1	LP012
HNIA	Mammary Gland	pSport1	LP012
HNJB	Palate carcinoma	pSport1	LP012
HNKA	Palate normal	pSport1	LP012
HMZA	Pharynx carcinoma	pSportI	LP012
HABG	Cheek Carcinoma	pSport1	LP012
НМZМ	Pharynx Carcinoma	pSport1	LP012 .
HDRM	Larynx Carcinoma	pSport1	LP012
HVAA	Pancreas normal PCA4 No	pSport1	LP012
HICA	Tongue carcinoma	pSport1	LP012
HUKA HUKB HUKC HUKD HUKE	Human Uterine Cancer	Lambda ZAP II	LP013
HFFA	Human Fetal Brain, random primed	Lambda ZAP II	LP013
HTUA	Activated T-cell labeled with 4-thioluri	Lambda ZAP II	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP013
НМЕВ	Human microvascular Endothelial cells, fract. B	Lambda ZAP II	LP013 .
HUSH	Human Umbilical Vein Endothelial cells, fract. A, re-excision	Lambda ZAP II	LP013
HLQC HLQD	Hepatocellular tumor, re-excision	Lambda ZAP II	LP013
HTWJ HTWK HTWL	Resting T-cell, re-excision	Lambda ZAP II	LP013
HF6S	Human Whole 6 week Old Embryo (II), subt	pBluescript	LP013
HHPS	Human Hippocampus, subtracted	pBluescript	LP013
HLIS	LNCAP. differential expression	pBluescript	LP013
нінѕ нінт	Early Stage Human Lung, Subtracted	pBluescript	LP013
HSUS	Supt cells, cyclohexamide treated, subtracted	pBluescript	LP013
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBluescript	LP013
HSDS	H. Striatum Depression, subtracted	pBluescript	LP013
HPTZ	Human Pituitary, Subtracted VII	pBluescript	LP013
HSDX	H. Striatum Depression, subt II	pBluescript	LP013
HSDZ	H. Striatum Depression, subt	pBluescript	LP013
НРВА НРВВ НРВС НРВО НРВЕ	Human Pineal Gland	pBluescript SK-	LP013
HRTA	Colorectal Tumor	pBluescript SK-	LP013
HSBA HSBB HSBC HSBM	HSC172 cells	pBluescript SK-	LP013
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBluescript SK-	LP013
НЈВА НЈВВ НЈВС НЈВД	Jurkat T-cell, S1 phase	pBluescript SK-	LP013
HTNA HTNB	Human Thyroid	pBluescript SK-	LP013
НАНА НАНВ	Human Adult Heart	Uni-ZAP XR	LP013
HE6A	Whole 6 week Old Embryo	Uni-ZAP XR	LP013
HFCA HFCB HFCC HFCD HFCE	Human Fetal Brain	Uni-ZAP XR	LP013
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP013
HGBA HGBD HGBE HGBF HGBG	Human Gall Bladder	Uni-ZAP XR	LP013
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP013
HTEA HTEB HTEC HTED HTEE	Human Testes	Uni-ZAP XR	LP013
HTTA HTTB HTTC HTTD HTTE	Human Testes Tumor	Uni-ZAP XR	LP013
НҮВА НҮВВ	Human Fetal Bone	Uni-ZAP XR	LP013
HFLA	Human Fetal Liver	Uni-ZAP XR	LP013
HHFB HHFC HHFD HHFE HHFF	Human Fetal Heart	Uni-ZAP XR	LP013
HUVB HUVC HUVD HUVE	Human Umbilical Vein, End. remake	Uni-ZAP XR	LP013
НТНВ НТНС HTHD	Human Thymus	Uni-ZAP XR	LP013
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP013
HTAA HTAB HTAC HTAD HTAE	Human Activated T-cells	Uni-ZAP XR	LP013
HFEA HFEB HFEC	Human Fetal Epithelium (skin)	Uni-ZAP XR	LP013
HIPA HIPB HIPC HIPD	Human Jurkat Membrane Bound Polysomes	Uni-ZAP XR	LP013
HESA	Human Epithelioid Sarcoma	Uni-ZAP XR	LP013
HALS	Human Adult Liver, Subtracted	Uni-ZAP XR	LP013
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP013
НСАА НСАВ НСАС	Cem cells, cyclohexamide treated	Uni-ZAP XR	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP013
НЕ9А НЕ9В НЕ9С НЕ9D НЕ9Е	Nine Week Old Early Stage Human	Uni-ZAP XR	LP013
HSFA	Human Fibrosarcoma	Uni-ZAP XR	LP013
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP013
HTRA	Human Trachea Tumor	Uni-ZAP XR	LP013
HE2A HE2D HE2E HE2H HE2I	12 Week Old Early Stage Human	Uni-ZAP XR	LP013
HE2B HE2C HE2F HE2G HE2P	12 Week Old Early Stage Human, II	Uni-ZAP XR	LP013
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP013
HBGA	Human Primary Breast Cancer	Uni-ZAP XR	LP013
НРТЅ НРТТ НРТО	Human Pituitary, subtracted	Uni-ZAP XR	LP013
HMQA HMQB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP013
НОАА НОАВ НОАС	Human Osteosarcoma	Uni-ZAP XR	LP013
HTOA HTOD HTOE HTOF HTOG	human tonsils	Uni-ZAP XR	LP013
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP013
НОРВ	Human OB HOS control fraction I	Uni-ZAP XR	LP013
HOQB	Human OB HOS treated (1 nM E2) fraction I	Uni-ZAP XR	LP013
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP013
HAQA HAQB HAQC HAQD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP013
HROA HROC	HUMAN STOMACH	Uni-ZAP XR	LP013
НВЈА НВЈВ НВЈС НВЈО НВЈЕ	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP013
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP013
НСРА	Corpus Callosum	Uni-ZAP XR	LP013
HSOA	stomach cancer (human)	Uni-ZAP XR	LP013
HERA	SKIN	Uni-ZAP XR	LP013
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP013
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP013
HWTA HWTB HWTC	wilm's tumor	Uni-ZAP XR	LP013
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP013
HAPN HAPO HAPP HAPQ HAPR	Human Adult Pulmonary;re-excision	Uni-ZAP XR	LP013
HLTG HLTH	Human T-cell lymphoma;re-excision	Uni-ZAP XR	LP013
HAHC HAHD HAHE	Human Adult Heart;re-excision	Uni-ZAP XR	LP013
HAGA HAGB HAGC HAGD HAGE	Human Amygdala	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP013
НЅНА НЅНВ НЅНС	Smooth muscle, IL1b induced	Uni-ZAP XR	LP013
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP013
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP013
НРЈА НРЈВ НРЈС	PC3 Prostate cell line	Uni-ZAP XR	LP013
НВТА	Bone Marrow Stroma, TNF&LPS ind	Uni-ZAP XR	LP013
HMCF HMCG HMCH HMCI HMCJ	Macrophage-oxLDL; re-excision	Uni-ZAP XR	LP013
HAGG HAGH HAGI	Human Amygdala;re-excision	Uni-ZAP XR	LP013
НАСА	H. Adipose Tissue	Uni-ZAP XR	LP013
HKFB	K562 + PMA (36 hrs),re-excision	ZAP Express	LP013
HCWT HCWU HCWV	CD34 positive cells (cord blood),re-ex	ZAP Express	LP013
HBWA	Whole brain	ZAP Express	LP013
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HAVM	Temporal cortex-Alzheizmer	pT-Adv	. LP014
HAVT	Hippocampus. Alzheimer Subtracted	pT-Adv	LP014
HHAS	CHME Cell Line	Uni-ZAP XR	LP014
HAJR	Larynx normal	pSport 1	LP014
HWLE HWLF HWLG HWLH	Colon Normal	pSport I	LP014
HCRM HCRN HCRO	Colon Carcinoma	pSport 1	LP014
HWLI HWLJ HWLK	Colon Normal	pSport 1	LP014
HWI THWLR HWLS HWLT	Colon Tumor	pSport 1	LP014
нвгм	Gastrocnemius Muscle	pSport I	LP014
HBOD HBOE	Quadriceps Muscle	pSport 1	LP014
НВКD НВКЕ	Soleus Muscle	pSport 1	LP014
НССМ	Pancreatic Langerhans	pSport 1	LP014
HWGA	Larynx carcinoma	pSport 1	LP014
HWGM HWGN	Larynx carcinoma	pSport 1	LP014
HWLA HWLB HWLC	Normal colon	pSport 1	LP014
HWLM HWLN	Colon Tumor	pSport 1	LP014
HVAM HVAN HVAO	Pancreas Tumor	pSport 1	LP014
НWGQ	Larynx carcinoma	pSport 1	LP014
HAQM HAQN	Salivary Gland	pSport 1	LP014
HASM	Stomach; normal	pSport 1	LP014
нвсм	Uterus; normal	pSport 1	LP014
НСDM	Testis; normal	pSport I	LP014
HDJM	Brain; normal	pSport 1	LP014
HEFM	Adrenal Gland, normal	pSport 1	LP014
НВАА	Rectum normal	pSport 1	LP014
HFDM	Recturn tumour	pSport 1	LP014
HGAM	Colon, normal	pSport 1	LP014
ннмм	Colon, tumour	pSport 1	LP014
HCLB HCLC	Human Lung Cancer	Lambda Zap II	LP015
HRLA	L1 Cell line	ZAP Express	LP015
ННАМ	Hypothalamus, Alzheimer's	pCMVSport 3.0	LP015
НКВА	Ku 812F Basophils Line	pSport 1	LP015
HS2S	Saos2, Dexamethosome Treated	pSport 1	LP016
HASA	Lung Carcinoma A549 TNFalpha activated	pSport 1	LP016
НТГМ	TF-1 Cell Line GM-CSF Treated	pSport 1	LP016
HYAS	Thyroid Tumour	pSport 1	LP016
HUTS	Larynx Normal	pSport 1	LP016
HXOA	Larynx Tumor	pSport l	LP016
НЕАН	Ea.hy.926 cell line	pSport 1	LP016
HINA	Adenocarcinoma Human	pSport 1	LP016
HRMA	Lung Mesothelium	pSport 1	LP016
HLCL	Human Pre-Differentiated Adipocytes	Uni-Zap XR	LP017
HS2A	Saos2 Cells	pSport I	LP020
HS2I	Saos2 Cells; Vitamin D3 Treated	pSport I	LP020
НИСМ	CHME Cell Line, untreated	pSport I	LP020
HEPN	Aryepiglottis Normal	pSport I	LP020

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HPSN	Sinus Piniformis Turnour	pSport I	LP020
HNSA	Stomach Normal	pSport I	LP020
HNSM	Stomach Tumour	pSport 1	LP020
HNLA	Liver Normal Met5No	pSport I	LP020
HUTA	Liver Tumour Met 5 Tu	pSport 1	LP020
HOCN	Colon Normal	pSport I	LP020
HOCT	Colon Tumor	pSport 1	LP020
HTNT	Tongue Tumour	pSport 1	LP020
HLXN	Larynx Normal	pSport I	LP020
HLXT	Larynx Tumour	pSport I	LP020
HTYN	Thymus	pSport I	LP020
HPLN	Placenta	pSport I	LP020
HTNG	Tongue Normal	pSport I	LP020
HZAA	Thyroid Normal (SDCA2 No)	pSport I	LP020
HWES	Thyroid Thyroiditis	pSport I	LP020
HFHD	Ficolled Human Stromal Cells, 5Fu treated	pTrip1Ex2	LP021
ненм,нени	Ficolled Human Stromal Cells, Untreated	pTrip1Ex2	LP021
HPCI	Hep G2 Cells, lambda library	lambda Zap-CMV XR	LP021
НВСА,НВСВ.НВСС	H. Lymph node breast Cancer	Uni-ZAP XR	LP021
HCOK	Chondrocytes	pSPORT1	LP022
HDCA, HDCB, HDCC	Dendritic Cells From CD34 Cells	pSPORT1	LP022
HDMA, HDMB	CD40 activated monocyte dendritic cells	pSPORT1	LP022
HDDM, HDDN, HDDO	LPS activated derived dendritic cells	pSPORT1	LP022
HPCR	Hep G2 Cells, PCR library	lambda Zap-CMV XR	LP022
НААА, НААВ, НААС	Lung, Cancer (4005313A3): Invasive Poorly Differentiated Lung Adenocarcinoma	pSPORTI	LP022
НІРА, НІРВ, НІРС	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	pSPORT1	LP022
ноон, нооі	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot	pSPORT1	LP022
HIDA	Lung, Normal: (4005313 B1)	pSPORTI	LP022
HUJA,HUJB,HUJC,HUJD,HUJE	B-Cells	pCMVSport 3.0	LP022
HNOA,HNOB,HNOC,HNOD	Ovary, Normal: (9805C040R)	pSPORT1	LP022
INLM	Lung, Normal: (4005313 B1)	pSPORT1	LP022
HSCL	Stromai Cells	pSPORT1	LP022
HAAX	Lung, Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic lung adenocarcinoma	pSPORT1	LP022
HUUA,HUUB,HUUC,HUUD	B-cells (unstimulated)	pTrip1Ex2	LP022
HWWA,HWWB,HWWC,HWWD,HW WE,HWWF,HWWG		pSPORT1	LP022
HCCC	Colon, Cancer: (9808C064R)	pCMVSport 3.0	LP023
HPDO HPDP HPDQ HPDR HPD	Ovary, Cancer (9809C332): Poorly	pSport 1	LP023
	differentiated adenocarcinoma		

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
НРСО НРСР НРСQ НРСТ	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	pSport 1	LP023
носм носо носр носо	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	pSport i	LP023
НСВМ НСВО	Breast, Cancer: (4004943 A5)	pSport I	LP023
HNBT HNBU HNBV	Breast, Normal: (4005522B2)	pSport I	LP023
НВСР НВСО	Breast, Cancer: (4005522 A2)	pSport 1	LP023
НВСЈ	Breast, Cancer: (9806C012R)	pSport 1	LP023
HSAM HSAN	Stromal cells 3.88	pSport 1	LP023
HVCA HVCB HVCC HVCD	Ovary, Cancer: (4004332 A2)	pSport I	LP023
HSCK HSEN HSEO	Stromal cells (HBM3.18)	pSport I	LP023
HSCP HSCQ	stromal cell clone 2.5	pSport 1	LP023
HUXA	Breast Cancer: (4005385 A2)	pSport 1	LP023
нсом нсоо нсор нсоо	Ovary, Cancer (4004650 A3): Well- Differentiated Micropapillary Serous Carcinoma	pSport I	LP023
НВИМ	Breast, Cancer: (9802C020E)	pSport I	LP023
HVVA HVVB HVVC HVVD HVVE	Human Bone Marrow, treated	pSport 1	LP023

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Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 5. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to the nucleotide sequence of SEQ ID NO:X.

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Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ³²P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the nucleotide sequence of SEQ ID NO:X are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 µl of reaction mixture with 0.5 ug of the above cDNA template. A convenient reaction mixture is 1.5-5 mM MgCl₂, 0.01% (w/v) gelatin, 20 µM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not

limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., Nucleic Acids Res. 21(7):1683-1684 (1993).)

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Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the sequence corresponding to SEQ ID NO:X, according to the method described in Example 1. (See also, Sambrook.)

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Example 3: Tissue specific expression analysis

The Human Genome Sciences, Inc. (HGS) database is derived from sequencing tissue specific cDNA libraries. Libraries generated from a particular tissue are selected and the specific tissue expression pattern of EST groups or assembled contigs within these libraries is determined by comparison of the expression patterns of those groups or contigs within the entire database. ESTs which show tissue specific expression are selected.

The original clone from which the specific EST sequence was generated, is obtained from the catalogued library of clones and the insert amplified by PCR using methods known in the art. The PCR product is denatured then transferred in 96 well format to a nylon membrane (Schleicher and Scheull) generating an array filter of tissue specific clones. Housekeeping genes, maize genes, and known tissue specific genes are included on the filters. These targets can be used in signal normalization and to validate assay sensitivity. Additional targets are included to monitor probe length and specificity of hybridization.

Radioactively labeled hybridization probes are generated by first strand cDNA synthesis per the manufacturer's instructions (Life Technologies) from mRNA/RNA samples prepared from the specific tissue being analyzed. The hybridization probes are purified by gel exclusion chromatography, quantitated, and hybridized with the array filters in hybridization bottles at 65°C overnight. The filters are washed under stringent conditions and signals are captured using a Fuji phosphorimager.

Data is extracted using AIS software and following background subtraction, signal normalization is performed. This includes a normalization of filter-wide expression levels between different experimental runs. Genes that are differentially expressed in the tissue of interest are identified and the full length sequence of these clones is generated.

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Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions: 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute

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cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

Example 5: Bacterial Expression of a Polypeptide

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A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.⁶⁰⁰) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., supra). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., supra).

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Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM immidazole. Immidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction

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sites for Ndel (5' primer) and Xbal, BamHl, Xhol, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

Example 6: Purification of a Polypeptide from an Inclusion Body

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The following alternative method can be used to purify a polypeptide expressed in E coli when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfuidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A₂₈₀ monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 µg of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System

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In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak Drosophila promoter in the same orientation, followed by the

polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., Virology 170:31-39 (1989).

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Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon, is amplified using the PCR protocol described in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("Geneclean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. E. coli HB101 or other suitable E. coli hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five μg of a plasmid containing the polynucleotide is co-transfected with 1.0 μg of a commercially available linearized baculovirus DNA ("BaculoGoldTM baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc.

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Natl. Acad. Sci. USA 84:7413-7417 (1987). One μg of BaculoGoldTM virus DNA and 5 μg of the plasmid are mixed in a sterile well of a microtiter plate containing 50 μl of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 μl Lipofectin plus 90 μl Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

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After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 μ Ci of ³⁵S-methionine and 5 μ Ci ³⁵S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

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Example 8: Expression of a Polypeptide in Mammalian Cells

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The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSport 2.0, and pCMVSport 3.0. Mammalian host cells that could be used include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as DHFR, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No.209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

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A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the vector does not need a second signal peptide. Alternatively, if a naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five µg of the expression plasmid pC6 or pC4 is cotransfected with 0.5 µg of the plasmid pSVneo using lipofectin (Felgner et al., supra). The plasmid pSV2-neo contains a dominant selectable marker, the neo gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of metothrexate plus 1 mg/ml G418. After about 10-14 days single clones

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are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 μ M, 2 μ M, 5 μ M, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 μ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

Example 9: Protein Fusions

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The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the halflife time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the nonfused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without

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a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the polypeptide of the present invention, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

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GGGATCCGGAGCCCAAATCTTCTGACAAAACTCACACATGCCCACCGTGCCCAG CACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGA 10 CACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGTGGACGTAAGC CACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCAT AATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC AGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGC AAGGTCTCCAACAAGCCCTCCCAACCCCCATCGAGAAAACCATCTCCAAAGCC AAAGGGCAGCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAG 15 CTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAAGC GACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGAC CACGCCTCCGTGCTGGACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACC GTGGACAGGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCAT 20 GAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAAT GAGTGCGACGCCGCGACTCTAGAGGAT (SEQ ID NO:1685)

Example 10: Production of an Antibody from a Polypeptide

25 a) Hybridoma Technology

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The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) As one example of such methods, cells expressing polypeptide of the present invention are administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of polypeptide of the present invention is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

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Monoclonal antibodies specific for polypeptide of the present invention are prepared using hybridoma technology. (Kohler et al., Nature 256:495 (1975); Kohler et al., Eur. J. Immunol. 6:511 (1976); Kohler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981)). In general, an animal (preferably a mouse) is immunized with polypeptide of the present invention or, more preferably, with a secreted polypeptide of the present invention-expressing cell. Such polypeptide-expressing cells are cultured in any suitable tissue culture medium, preferably in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

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The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (Gastroenterology 80:225-232 (1981)). The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide of the present invention.

Alternatively, additional antibodies capable of binding to polypeptide of the present invention can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the polypeptide of the present invention-specific antibody can be blocked by polypeptide of the present invention. Such antibodies comprise anti-idiotypic antibodies to the polypeptide of the present invention-specific antibody and are used to immunize an animal to induce formation of further polypeptide of the present invention-specific antibodies.

For in vivo use of antibodies in humans, an antibody is "humanized". Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric and humanized

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antibodies are known in the art and are discussed herein. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

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b) Isolation Of Antibody Fragments Directed Against Polypeptide of the Present Invention From A Library Of scFvs

Naturally occurring V-genes isolated from human PBLs are constructed into a library of antibody fragments which contain reactivities against polypeptide of the present invention to which the donor may or may not have been exposed (see e.g., U.S. Patent 5,885,793 incorporated herein by reference in its entirety).

Rescue of the Library. A library of scFvs is constructed from the RNA of human PBLs as described in PCT publication WO 92/01047. To rescue phage displaying antibody fragments, approximately 109 E. coli harboring the phagemid are used to inoculate 50 ml of 2xTY containing 1% glucose and 100 μg/ml of ampicillin (2xTY-AMP-GLU) and grown to an O.D. of 0.8 with shaking. Five ml of this culture is used to innoculate 50 ml of 2xTY-AMP-GLU, 2 x 108 TU of delta gene 3 helper (M13 delta gene III, see PCT publication WO 92/01047) are added and the culture incubated at 37°C for 45 minutes without shaking and then at 37°C for 45 minutes with shaking. The culture is centrifuged at 4000 r.p.m. for 10 min. and the pellet resuspended in 2 liters of 2xTY containing 100 μg/ml ampicillin and 50 ug/ml kanamycin and grown overnight. Phage are prepared as described in PCT publication WO 92/01047.

M13 delta gene III is prepared as follows: M13 delta gene III helper phage does not encode gene III protein, hence the phage(mid) displaying antibody fragments have a greater avidity of binding to antigen. Infectious M13 delta gene III particles are made by growing the helper phage in cells harboring a pUC19 derivative supplying the wild type gene III protein during phage morphogenesis. The culture is incubated for 1 hour at 37° C without shaking and then for a further hour at 37°C with shaking. Cells are spun down (IEC-Centra 8,400 r.p.m. for 10 min), resuspended in 300 ml 2xTY broth containing 100 µg ampicillin/ml and 25 µg kanamycin/ml (2xTY-AMP-KAN) and grown overnight, shaking at 37°C. Phage particles are purified and concentrated from the culture medium by two PEG-precipitations

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(Sambrook et al., 1990), resuspended in 2 ml PBS and passed through a 0.45 µm filter (Minisart NML; Sartorius) to give a final concentration of approximately 1013 transducing units/ml (ampicillin-resistant clones).

Panning of the Library. Immunotubes (Nunc) are coated overnight in PBS with 4 ml of either 100 μg/ml or 10 μg/ml of a polypeptide of the present invention. Tubes are blocked with 2% Marvel-PBS for 2 hours at 37°C and then washed 3 times in PBS. Approximately 1013 TU of phage is applied to the tube and incubated for 30 minutes at room temperature tumbling on an over and under turntable and then left to stand for another 1.5 hours. Tubes are washed 10 times with PBS 0.1% Tween-20 and 10 times with PBS. Phage are eluted by adding 1 ml of 100 mM triethylamine and rotating 15 minutes on an under and over turntable after which the solution is immediately neutralized with 0.5 ml of 1.0M Tris-HCl, pH 7.4. Phage are then used to infect 10 ml of mid-log E. coli TG1 by incubating eluted phage with bacteria for 30 minutes at 37°C. The E. coli are then plated on TYE plates containing 1% glucose and 100 μg/ml ampicillin. The resulting bacterial library is then rescued with delta gene 3 helper phage as described above to prepare phage for a subsequent round of selection. This process is then repeated for a total of 4 rounds of affinity purification with tube-washing increased to 20 times with PBS, 0.1% Tween-20 and 20 times with PBS for rounds 3 and 4.

Characterization of Binders. Eluted phage from the 3rd and 4th rounds of selection are used to infect E. coli HB 2151 and soluble scFv is produced (Marks, et al., 1991) from single colonies for assay. ELISAs are performed with microtitre plates coated with either 10 pg/ml of the polypeptide of the present invention in 50 mM bicarbonate pH 9.6. Clones positive in ELISA are further characterized by PCR fingerprinting (see, e.g., PCT publication WO 92/01047) and then by sequencing. These ELISA positive clones may also be further characterized by techniques known in the art, such as, for example, epitope mapping, binding affinity, receptor signal transduction, ability to block or competitively inhibit antibody/antigen binding, and competitive agonistic or antagonistic activity.

Example 11: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

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RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X; and/or the nucleotide sequence of the related cDNA in the cDNA clone contained in a deposited library. Suggested PCR conditions consist of 35 cycles at 95 degrees C for 30 seconds; 60-120 seconds at 52-58 degrees C; and 60-120 seconds at 70 degrees C, using buffer solutions described in Sidransky et al., Science 252:706 (1991).

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PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton et al., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Manheim), and FISH performed as described in Johnson et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an

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associated disease.

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Example 12: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 13: Formulation

The invention also provides methods of treatment and/or prevention of diseases or disorders (such as, for example, any one or more of the diseases or disorders disclosed

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herein) by administration to a subject of an effective amount of a Therapeutic. By therapeutic is meant a polynucleotides or polypeptides of the invention (including fragments and variants), agonists or antagonists thereof, and/or antibodies thereto, in combination with a pharmaceutically acceptable carrier type (e.g., a sterile carrier).

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The Therapeutic will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the Therapeutic alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of the Therapeutic administered parenterally per dose will be in the range of about lug/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the Therapeutic is typically administered at a dose rate of about 1 ug/kg/hour to about 50 ug/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Therapeutics can be are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler,

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diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics include suitable polymeric materials (such as, for example, semi-permeable polymer matrices in the form of shaped articles, e.g., films, or mirocapsules), suitable hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, and sparingly soluble derivatives (such as, for example, a sparingly soluble salt).

Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman et al., Biopolymers 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (Langer et al., J. Biomed. Mater. Res. 15:167-277 (1981), and Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (Langer et al., Id.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988).

Sustained-release Therapeutics also include liposomally entrapped Therapeutics of the invention (see generally, Langer, Science 249:1527-1533 (1990); Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 317 -327 and 353-365 (1989)). Liposomes containing the Therapeutic are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. (USA) 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. (USA) 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal Therapeutic.

In yet an additional embodiment, the Therapeutics of the invention are delivered by way of a pump (see Langer, supra; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

For parenteral administration, in one embodiment, the Therapeutic is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form

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(solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to the Therapeutic.

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Generally, the formulations are prepared by contacting the Therapeutic uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The Therapeutic is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any pharmaceutical used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutics generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Therapeutics ordinarily will be stored in unit or multi-dose containers, for example,

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sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous Therapeutic solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized Therapeutic using bacteriostatic Water-for-Injection.

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The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the Therapeutics of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the Therapeutics may be employed in conjunction with other therapeutic compounds.

The Therapeutics of the invention may be administered alone or in combination with adjuvants. Adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, alum, alum plus deoxycholate (ImmunoAg), MTP-PE (Biocine Corp.), QS21 (Genentech, Inc.), BCG, and MPL. In a specific embodiment, Therapeutics of the invention are administered in combination with alum. In another specific embodiment, Therapeutics of the invention are administered in combination with OS-21. Further adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, Monophosphoryl lipid immunomodulator, AdjuVax 100a, QS-21, QS-18, CRL1005, Aluminum salts, MF-59, and Virosomal adjuvant technology. Vaccines that may be administered with the Therapeutics of the invention include, but are not limited to, vaccines directed toward protection against MMR (measles, mumps, rubella), polio, varicella, tetanus/diptheria, hepatitis A, hepatitis B, haemophilus influenzae B, whooping cough, pneumonia, influenza, Lyme's Disease, rotavirus, cholera, yellow fever, Japanese encephalitis, poliomyelitis, rabies, typhoid fever, and pertussis. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

The Therapeutics of the invention may be administered alone or in combination with other therapeutic agents. Therapeutic agents that may be administered in combination with the Therapeutics of the invention, include but not limited to, other members of the TNF family, chemotherapeutic agents, antibiotics, steroidal and non-steroidal anti-inflammatories, conventional immunotherapeutic agents, cytokines and/or growth factors. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

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In one embodiment, the Therapeutics of the invention are administered in combination with members of the TNF family. TNF, TNF-related or TNF-like molecules that may be administered with the Therapeutics of the invention include, but are not limited to, soluble forms of TNF-alpha, lymphotoxin-alpha (LT-alpha, also known as TNF-beta), LT-beta (found in complex heterotrimer LT-alpha2-beta), OPGL, FasL, CD27L, CD30L, CD40L, 4-1BBL, DcR3, OX40L, TNF-gamma (International Publication No. WO 96/14328), AIM-I (International Publication No. WO 97/33899), endokine-alpha (International Publication No. WO 98/07880), TR6 (International Publication No. WO 98/30694), OPG, and neutrokine-alpha (International Publication No. WO 98/18921, OX40, and nerve growth factor (NGF), and soluble forms of Fas, CD30, CD27, CD40 and 4-IBB, TR2 (International Publication No. WO 96/34095), DR3 (International Publication No. WO 97/33904), DR4 (International Publication No. WO 98/32856), TR5 (International Publication No. WO 98/30693), TR6 (International Publication No. WO 98/30694), TR7 (International Publication No. WO 98/41629), TRANK, TR9 (International Publication No. WO 98/56892),TR10 (International Publication No. WO 98/54202), 312C2 (International Publication No. WO 98/06842), and TR12, and soluble forms CD154, CD70, and CD153.

In certain embodiments, Therapeutics of the invention are administered in combination with antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors. Nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, RETROVIRTM (zidovudine/AZT), VIDEXTM

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(didanosine/ddI), HIVID™ (zalcitabine/ddC), ZERIT™ (stavudine/d4T), EPIVIR™ (lamivudine/3TC), and COMBIVIR™ (zidovudine/lamivudine). Non-nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, VIRAMUNE™ (nevirapine), RESCRIPTOR™ (delavirdine), and SUSTIVA™ (efavirenz). Protease inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, CRIXIVAN™ (indinavir), NORVIR™ (ritonavir), INVIRASE™ (saquinavir), and VIRACEPT™ (nelfinavir). In a specific embodiment, antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors may be used in any combination with Therapeutics of the invention to treat AIDS and/or to prevent or treat HIV infection.

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In other embodiments, Therapeutics of the invention may be administered in combination with anti-opportunistic infection agents. Anti-opportunistic agents that may be administered in combination with the Therapeutics of the invention, include, but are not TRIMETHOPRIM-SULFAMETHOXAZOLE", DAPSONE", 15 limited to, PENTAMIDINE™, ATOVAQUONE™, ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, ETHAMBUTOL™, RIFABUTIN™, CLARITHROMYCIN™, AZITHROMYCIN™, GANCICLOVIR™, FOSCARNET™, CIDOFOVIR™, FLUCONAZOLE™, ITRACONAZOLE™, KETOCONAZOLE™, ACYCLOVIR™, FAMCICOLVIR™, PYRIMETHAMINE™, LEUCOVORIN™, NEUPOGEN™ (filgrastim/G-CSF), and 20 LEUKINE™ (sargramostim/GM-CSF). In a specific embodiment, Therapeutics of the invention are used in any combination with TRIMETHOPRIM-SULFAMETHOXAZOLE TO, DAPSONE™, PENTAMIDINE™, and/or ATOVAQUONE™ to prophylactically treat or prevent an opportunistic Pneumocystis carinii pneumonia infection. In another specific 25 embodiment, Therapeutics of the invention are used in any combination with ISONIAZIDTM, RIFAMPIN™, PYRAZINAMIDE™, and/or ETHAMBUTOL™ to prophylactically treat or prevent an opportunistic Mycobacterium avium complex infection. In another specific embodiment, Therapeutics of the invention are used in any combination with RIFABUTIN™, CLARITHROMYCIN™, and/or AZITHROMYCIN™ to prophylactically treat or prevent an 30 opportunistic Mycobacterium tuberculosis infection. In another specific embodiment, Therapeutics of the invention are used in any combination with GANCICLOVIRTM,

FOSCARNET™, and/or CIDOFOVIR™ to prophylactically treat or prevent an opportunistic cytomegalovirus infection. In another specific embodiment, Therapeutics of the invention are used in any combination with FLUCONAZOLE™, ITRACONAZOLE™, and/or KETOCONAZOLE™ to prophylactically treat or prevent an opportunistic fungal infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ACYCLOVIR™ and/or FAMCICOLVIR™ to prophylactically treat or prevent an opportunistic herpes simplex virus type I and/or type II infection. In another specific embodiment, Therapeutics of the invention are used in any combination with PYRIMETHAMINE™ and/or LEUCOVORIN™ to prophylactically treat or prevent an opportunistic Toxoplasma gondii infection. In another specific embodiment, Therapeutics of the invention are used in any combination with LEUCOVORIN™ and/or NEUPOGEN™ to prophylactically treat or prevent an opportunistic bacterial infection.

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In a further embodiment, the Therapeutics of the invention are administered in combination with an antiviral agent. Antiviral agents that may be administered with the Therapeutics of the invention include, but are not limited to, acyclovir, ribavirin, amantadine, and remantidine.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antibiotic agent. Antibiotic agents that may be administered with the Therapeutics of the invention include, but are not limited to, amoxicillin, beta-lactamases, aminoglycosides, beta-lactam (glycopeptide), beta-lactamases, Clindamycin, chloramphenicol, cephalosporins, ciprofloxacin, ciprofloxacin, erythromycin, fluoroquinolones, macrolides, metronidazole, penicillins, quinolones, rifampin, streptomycin, sulfonamide, tetracyclines, trimethoprim, trimethoprim-sulfamthoxazole, and vancomycin.

Conventional nonspecific immunosuppressive agents, that may be administered in combination with the Therapeutics of the invention include, but are not limited to, steroids, cyclosporine, cyclosporine analogs, cyclophosphamide methylprednisone, prednisone, azathioprine, FK-506, 15-deoxyspergualin, and other immunosuppressive agents that act by suppressing the function of responding T cells.

In specific embodiments, Therapeutics of the invention are administered in combination with immunosuppressants. Immunosuppressants preparations that may be administered with the Therapeutics of the invention include, but are not limited to, ORTHOCLONETM (OKT3), SANDIMMUNETM/NEORALTM/SANGDYATM (cyclosporin),

PROGRAF™ (tacrolimus), CELLCEPT™ (mycophenolate), Azathioprine, glucorticosteroids, and RAPAMUNE™ (sirolimus). In a specific embodiment, immunosuppressants may be used to prevent rejection of organ or bone marrow transplantation.

In an additional embodiment, Therapeutics of the invention are administered alone or in combination with one or more intravenous immune globulin preparations. Intravenous immune globulin preparations that may be administered with the Therapeutics of the invention include, but not limited to, GAMMAR™, IVEEGAM™, SANDOGLOBULIN™, GAMMAGARD S/D™, and GAMIMUNE™. In a specific embodiment, Therapeutics of the invention are administered in combination with intravenous immune globulin preparations in transplantation therapy (e.g., bone marrow transplant).

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In an additional embodiment, the Therapeutics of the invention are administered alone or in combination with an anti-inflammatory agent. Anti-inflammatory agents that may be administered with the Therapeutics of the invention include, but are not limited to, glucocorticoids and the nonsteroidal anti-inflammatories, aminoarylcarboxylic acid derivatives, arylacetic acid derivatives, arylbutyric acid derivatives, arylcarboxylic acids, arylpropionic acid derivatives, pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, e-acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, nimesulide, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

In another embodiment, compostions of the invention are administered in combination with a chemotherapeutic agent. Chemotherapeutic agents that may be administered with the Therapeutics of the invention include, but are not limited to, antibiotic derivatives (e.g., doxorubicin, bleomycin, daunorubicin, and dactinomycin); antiestrogens (e.g., tamoxifen); antimetabolites (e.g., fluorouracil, 5-FU, methotrexate, floxuridine, interferon alpha-2b, glutamic acid, plicamycin, mercaptopurine, and 6-thioguanine); cytotoxic agents (e.g., carmustine, BCNU, lomustine, CCNU, cytosine arabinoside, cyclophosphamide, estramustine, hydroxyurea, procarbazine, mitomycin, busulfan, cis-platin, and vincristine sulfate); hormones (e.g., medroxyprogesterone, estramustine phosphate sodium, ethinyl estradiol, estradiol, megestrol acetate, methyltestosterone, diethylstilbestrol diphosphate, chlorotrianisene, and testolactone); nitrogen mustard derivatives (e.g., mephalen, chorambucil, mechlorethamine (nitrogen mustard) and thiotepa); steroids and

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combinations (e.g., bethamethasone sodium phosphate); and others (e.g., dicarbazine, asparaginase, mitotane, vincristine sulfate, vinblastine sulfate, and etoposide).

In a specific embodiment, Therapeutics of the invention are administered in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or any combination of the components of CHOP. In another embodiment, Therapeutics of the invention are administered in combination with Rituximab. In a further embodiment, Therapeutics of the invention are administered with Rituxmab and CHOP, or Rituxmab and any combination of the components of CHOP.

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In an additional embodiment, the Therapeutics of the invention are administered in combination with cytokines. Cytokines that may be administered with the Therapeutics of the invention include, but are not limited to, IL2, IL3, IL4, IL5, IL6, IL7, IL10, IL12, IL13, IL15, anti-CD40, CD40L, IFN-gamma and TNF-alpha. In another embodiment, Therapeutics of the invention may be administered with any interleukin, including, but not limited to, IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, and IL-21.

In an additional embodiment, the Therapeutics of the invention are administered in combination with angiogenic proteins. Angiogenic proteins that may be administered with the Therapeutics of the invention include, but are not limited to, Glioma Derived Growth Factor (GDGF), as disclosed in European Patent Number EP-399816; Platelet Derived Growth Factor-A (PDGF-A), as disclosed in European Patent Number EP-682110; Platelet Derived Growth Factor-B (PDGF-B), as disclosed in European Patent Number EP-282317; Placental Growth Factor (PIGF), as disclosed in International Publication Number WO 92/06194; Placental Growth Factor-2 (PIGF-2), as disclosed in Hauser et al., Gorwth Factors, 4:259-268 (1993); Vascular Endothelial Growth Factor (VEGF), as disclosed in International Publication Number WO 90/13649; Vascular Endothelial Growth Factor-A (VEGF-A), as disclosed in European Patent Number EP-506477; Vascular Endothelial Growth Factor-2 (VEGF-2), as disclosed in International Publication Number WO 96/39515; Vascular Endothelial Growth Factor B (VEGF-3); Vascular Endothelial Growth Factor B-186 (VEGF-B186), as disclosed in International Publication Number WO 96/26736; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/02543; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/07832; and Vascular Endothelial Growth Factor-E (VEGF-E), as disclosed in German Patent Number DE19639601. The above mentioned references are incorporated herein by reference herein.

In an additional embodiment, the Therapeutics of the invention are administered in combination with hematopoietic growth factors. Hematopoietic growth factors that may be administered with the Therapeutics of the invention include, but are not limited to, LEUKINE™ (SARGRAMOSTIM™) and NEUPOGEN™ (FILGRASTIM™).

In an additional embodiment, the Therapeutics of the invention are administered in combination with Fibroblast Growth Factors. Fibroblast Growth Factors that may be administered with the Therapeutics of the invention include, but are not limited to, FGF-1, FGF-2, FGF-3, FGF-4, FGF-5, FGF-6, FGF-7, FGF-8, FGF-9, FGF-10, FGF-11, FGF-12, FGF-13, FGF-14, and FGF-15.

In additional embodiments, the Therapeutics of the invention are administered in combination with other therapeutic or prophylactic regimens, such as, for example, radiation therapy.

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Example 14: Method of Treating Decreased Levels of the Polypeptide

The present invention relates to a method for treating an individual in need of an increased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an agonist of the invention (including polypeptides of the invention). Moreover, it will be appreciated that conditions caused by a decrease in the standard or normal expression level of a polypeptide of the present invention in an individual can be treated by administering the agonist or antagonist of the present invention. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a Therapeutic comprising an amount of the agonist or antagonist to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the agonist or antagonist for six consecutive days. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 13.

Example 15: Method of Treating Increased Levels of the Polypeptide

The present invention also relates to a method of treating an individual in need of a decreased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an antagonist of the invention (including polypeptides and antibodies of the invention).

In one example, antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 13.

Example 16: Method of Treatment Using Gene Therapy-Ex Vivo

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One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37 degree C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using

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PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1 using primers and having appropriate restriction sites and initiation/stop codons, if necessary. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a subconfluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

Example 17: Gene Therapy Using Endogenous Genes Corresponding To Polynucleotides of the Invention

Another method of gene therapy according to the present invention involves operably

associating the endogenous polynucleotide sequence of the invention with a promoter via homologous recombination as described, for example, in U.S. Patent NO: 5,641,670, issued June 24, 1997; International Publication NO: WO 96/29411, published September 26, 1996; International Publication NO: WO 94/12650, published August 4, 1994; Koller et al., *Proc. Natl. Acad. Sci. USA*, 86:8932-8935 (1989); and Zijlstra et al., *Nature*, 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made which contain a promoter and targeting sequences, which are homologous to the 5' non-coding sequence of endogenous polynucleotide sequence, flanking the promoter. The targeting sequence will be sufficiently near the 5' end of the polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination. The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter.

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The amplified promoter and the amplified targeting sequences are digested with the appropriate restriction enzymes and subsequently treated with calf intestinal phosphatase. The digested promoter and digested targeting sequences are added together in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The construct is size fractionated on an agarose gel then purified by phenol extraction and ethanol precipitation.

In this Example, the polynucleotide constructs are administered as naked polynucleotides via electroporation. However, the polynucleotide constructs may also be administered with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, precipitating agents, etc. Such methods of delivery are known in the art.

Once the cells are transfected, homologous recombination will take place which results in the promoter being operably linked to the endogenous polynucleotide sequence. This results in the expression of polynucleotide corresponding to the polynucleotide in the cell. Expression may be detected by immunological staining, or any other method known in the art.

Fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in DMEM + 10% fetal calf serum. Exponentially growing or early stationary phase fibroblasts are trypsinized and rinsed from the plastic surface with nutrient medium. An aliquot of the cell suspension is removed for counting, and the remaining cells are subjected to centrifugation. The supernatant is aspirated and the pellet is resuspended in 5 ml of electroporation buffer (20 mM HEPES pH 7.3, 137 mM NaCl, 5 mM KCl, 0.7 mM Na₂ HPO₄, 6 mM dextrose). The cells are recentrifuged, the supernatant aspirated, and the cells resuspended in electroporation buffer containing 1 mg/ml acetylated bovine serum albumin. The final cell suspension contains approximately 3X10⁶ cells/ml. Electroporation should be performed immediately following resuspension.

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Plasmid DNA is prepared according to standard techniques. For example, to construct a plasmid for targeting to the locus corresponding to the polynucleotide of the invention, plasmid pUC18 (MBI Fermentas, Amherst, NY) is digested with HindIII. The CMV promoter is amplified by PCR with an XbaI site on the 5' end and a BamHI site on the 3'end. Two non-coding sequences are amplified via PCR: one non-coding sequence (fragment 1) is amplified with a HindIII site at the 5' end and an Xba site at the 3'end; the other non-coding sequence (fragment 2) is amplified with a BamHI site at the 5'end and a HindIII site at the 3'end. The CMV promoter and the fragments (1 and 2) are digested with the appropriate enzymes (CMV promoter - XbaI and BamHI; fragment 1 - XbaI; fragment 2 - BamHI) and ligated together. The resulting ligation product is digested with HindIII, and ligated with the HindIII-digested pUC18 plasmid.

Plasmid DNA is added to a sterile cuvette with a 0.4 cm electrode gap (Bio-Rad). The final DNA concentration is generally at least 120 μ g/ml. 0.5 ml of the cell suspension (containing approximately 1.5. $X10^6$ cells) is then added to the cuvette, and the cell suspension and DNA solutions are gently mixed. Electroporation is performed with a Gene-Pulser apparatus (Bio-Rad). Capacitance and voltage are set at 960 μ F and 250-300 V, respectively. As voltage increases, cell survival decreases, but the percentage of surviving cells that stably incorporate the introduced DNA into their genome increases dramatically. Given these parameters, a pulse time of approximately 14-20 mSec should be observed.

Electroporated cells are maintained at room temperature for approximately 5 min, and the contents of the cuvette are then gently removed with a sterile transfer pipette. The cells are added directly to 10 ml of prewarmed nutrient media (DMEM with 15% calf serum) in a

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10 cm dish and incubated at 37 degree C. The following day, the media is aspirated and replaced with 10 ml of fresh media and incubated for a further 16-24 hours.

The engineered fibroblasts are then injected into the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads. The fibroblasts now produce the protein product. The fibroblasts can then be introduced into a patient as described above.

Example 18: Method of Treatment Using Gene Therapy - In Vivo

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Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide. The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata et al., Cardiovasc. Res. 35(3):470-479 (1997); Chao et al., Pharmacol. Res. 35(6):517-522 (1997); Wolff, Neuromuscul. Disord. 7(5):314-318 (1997); Schwartz et al., Gene Ther. 3(5):405-411 (1996); Tsurumi et al., Circulation 94(12):3281-3290 (1996) (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) Ann. NY Acad. Sci. 772:126-139 and Abdallah B. et al. (1995) Biol. Cell 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that

allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to

arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 19: Transgenic Animals

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The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e.g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (i.e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e.g., Ulmer et al., Science 259:1745 (1993); introducing nucleic acid constructs into embryonic pleuripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, *i.e.*, mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, *e.g.*, head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci. USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of

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the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, *in situ* hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

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Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (E.g., see Smithies et al., Nature 317:230-234 (1985); Thomas & Capecchi, Cell 51:503-512 (1987); Thompson et al., Cell 5:313-321 (1989); each of which is incorporated by reference herein in its entirety). For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination. results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (e.g., see Thomas & Capecchi 1987 and Thompson 1989, supra). However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

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In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e.g., knockouts) are administered to a patient in vivo. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e.g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc. The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and

preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e.g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, <u>e.g.</u>, genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U.S. Patent No. 5,399,349; and Mulligan & Wilson, U.S. Patent No. 5,460,959 each of which is incorporated by reference herein in its entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

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Example 22: Assays Detecting Stimulation or Inhibition of B cell Proliferation and Differentiation

Generation of functional humoral immune responses requires both soluble and cognate signaling between B-lineage cells and their microenvironment. Signals may impart a positive stimulus that allows a B-lineage cell to continue its programmed development, or a negative stimulus that instructs the cell to arrest its current developmental pathway. To date, numerous stimulatory and inhibitory signals have been found to influence B cell responsiveness including IL-2, IL-4, IL-5, IL-6, IL-7, IL10, IL-13, IL-14 and IL-15. Interestingly, these signals are by themselves weak effectors but can, in combination with various co-stimulatory proteins, induce activation, proliferation, differentiation, homing, tolerance and death among B cell populations.

One of the best studied classes of B-cell co-stimulatory proteins is the TNF-superfamily. Within this family CD40, CD27, and CD30 along with their respective ligands CD154, CD70, and CD153 have been found to regulate a variety of immune responses. Assays which allow for the detection and/or observation of the proliferation and differentiation of these B-cell populations and their precursors are valuable tools in determining the effects various proteins may have on these B-cell populations in terms of proliferation and differentiation. Listed below are two assays designed to allow for the detection of the differentiation, proliferation, or inhibition of B-cell populations and their precursors.

In Vitro Assay- Agonists or antagonists of the invention can be assessed for its ability to induce activation, proliferation, differentiation or inhibition and/or death in B-cell populations and their precursors. The activity of the agonists or antagonists of the invention on purified human tonsillar B cells, measured qualitatively over the dose range from 0.1 to 10,000 ng/mL, is assessed in a standard B-lymphocyte co-stimulation assay in which purified tonsillar B cells are cultured in the presence of either formalin-fixed Staphylococcus aureus Cowan I (SAC) or immobilized anti-human IgM antibody as the priming agent. Second signals such as IL-2 and IL-15 synergize with SAC and IgM crosslinking to elicit B cell proliferation as measured by tritiated-thymidine incorporation. Novel synergizing agents can be readily identified using this assay. The assay involves isolating human tonsillar B cells by magnetic bead (MACS) depletion of CD3-positive cells. The resulting cell population is greater than 95% B cells as assessed by expression of CD45R(B220).

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Various dilutions of each sample are placed into individual wells of a 96-well plate to which are added 10⁵ B-cells suspended in culture medium (RPMI 1640 containing 10% FBS, 5 X 10⁻⁵M 2ME, 100U/ml penicillin, 10ug/ml streptomycin, and 10⁻⁵ dilution of SAC) in a total volume of 150ul. Proliferation or inhibition is quantitated by a 20h pulse (1uCi/well) with 3H-thymidine (6.7 Ci/mM) beginning 72h post factor addition. The positive and negative controls are IL2 and medium respectively.

In Vivo Assay- BALB/c mice are injected (i.p.) twice per day with buffer only, or 2 mg/Kg of agonists or antagonists of the invention, or truncated forms thereof. Mice receive this treatment for 4 consecutive days, at which time they are sacrificed and various tissues and serum collected for analyses. Comparison of H&E sections from normal spleens and spleens treated with agonists or antagonists of the invention identify the results of the activity

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of the agonists or antagonists on spleen cells, such as the diffusion of peri-arterial lymphatic sheaths, and/or significant increases in the nucleated cellularity of the red pulp regions, which may indicate the activation of the differentiation and proliferation of B-cell populations. Immunohistochemical studies using a B cell marker, anti-CD45R(B220), are used to determine whether any physiological changes to splenic cells, such as splenic disorganization, are due to increased B-cell representation within loosely defined B-cell zones that infiltrate established T-cell regions.

Flow cytometric analyses of the spleens from mice treated with agonist or antagonist is used to indicate whether the agonists or antagonists specifically increases the proportion of ThB+, CD45R(B220)dull B cells over that which is observed in control mice.

Likewise, a predicted consequence of increased mature B-cell representation in vivo is a relative increase in serum Ig titers. Accordingly, serum IgM and IgA levels are compared between buffer and agonists or antagonists-treated mice.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 23: T Cell Proliferation Assay

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A CD3-induced proliferation assay is performed on PBMCs and is measured by the 20 uptake of ³H-thymidine. The assay is performed as follows. Ninety-six well plates are coated with 100 µl/well of mAb to CD3 (HIT3a, Pharmingen) or isotype-matched control mAb (B33.1) overnight at 4 degrees C (1 µg/ml in .05M bicarbonate buffer, pH 9.5), then washed three times with PBS. PBMC are isolated by F/H gradient centrifugation from 25 human peripheral blood and added to quadruplicate wells (5 x 10⁴/well) of mAb coated plates in RPMI containing 10% FCS and P/S in the presence of varying concentrations of agonists or antagonists of the invention (total volume 200 ul). Relevant protein buffer and medium alone are controls. After 48 hr. culture at 37 degrees C, plates are spun for 2 min. at 1000 rpm and 100 µl of supernatant is removed and stored -20 degrees C for measurement of IL-2 30 (or other cytokines) if effect on proliferation is observed. Wells are supplemented with 100 ul of medium containing 0.5 uCi of ³H-thymidine and cultured at 37 degrees C for 18-24 hr. Wells are harvested and incorporation of ³H-thymidine used as a measure of proliferation.

Anti-CD3 alone is the positive control for proliferation. IL-2 (100 U/ml) is also used as a control which enhances proliferation. Control antibody which does not induce proliferation of T cells is used as the negative controls for the effects of agonists or antagonists of the invention.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

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Example 24: Effect of Agonists or Antagonists of the Invention on the Expression of MHC

Class II, Costimulatory and Adhesion Molecules and Cell Differentiation of Monocytes and

Monocyte-Derived Human Dendritic Cells

Dendritic cells are generated by the expansion of proliferating precursors found in the peripheral blood: adherent PBMC or elutriated monocytic fractions are cultured for 7-10 days with GM-CSF (50 ng/ml) and IL-4 (20 ng/ml). These dendritic cells have the characteristic phenotype of immature cells (expression of CD1, CD80, CD86, CD40 and MHC class II antigens). Treatment with activating factors, such as TNF-α, causes a rapid change in surface phenotype (increased expression of MHC class I and II, costimulatory and adhesion molecules, downregulation of FCγRII, upregulation of CD83). These changes correlate with increased antigen-presenting capacity and with functional maturation of the dendritic cells.

FACS analysis of surface antigens is performed as follows. Cells are treated 1-3 days with increasing concentrations of agonist or antagonist of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degrees C. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

Effect on the production of cytokines. Cytokines generated by dendritic cells, in particular IL-12, are important in the initiation of T-cell dependent immune responses. IL-12 strongly influences the development of Thl helper T-cell immune response, and induces cytotoxic T and NK cell function. An ELISA is used to measure the IL-12 release as follows. Dendritic cells (10⁶/ml) are treated with increasing concentrations of agonists or antagonists of the

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invention for 24 hours. LPS (100 ng/ml) is added to the cell culture as positive control. Supernatants from the cell cultures are then collected and analyzed for IL-12 content using commercial ELISA kit (e..g, R & D Systems (Minneapolis, MN)). The standard protocols provided with the kits are used.

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Effect on the expression of MHC Class II, costimulatory and adhesion molecules. Three major families of cell surface antigens can be identified on monocytes: adhesion molecules, molecules involved in antigen presentation, and Fc receptor. Modulation of the expression of MHC class II antigens and other costimulatory molecules, such as B7 and ICAM-1, may result in changes in the antigen presenting capacity of monocytes and ability to induce T cell activation. Increase expression of Fc receptors may correlate with improved monocyte cytotoxic activity, cytokine release and phagocytosis.

FACS analysis is used to examine the surface antigens as follows. Monocytes are treated 1-5 days with increasing concentrations of agonists or antagonists of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degreesC. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

Monocyte activation and/or increased survival. Assays for molecules that activate (or alternatively, inactivate) monocytes and/or increase monocyte survival (or alternatively, decrease monocyte survival) are known in the art and may routinely be applied to determine whether a molecule of the invention functions as an inhibitor or activator of monocytes. Agonists or antagonists of the invention can be screened using the three assays described below. For each of these assays, Peripheral blood mononuclear cells (PBMC) are purified from single donor leukopacks (American Red Cross, Baltimore, MD) by centrifugation through a Histopaque gradient (Sigma). Monocytes are isolated from PBMC by counterflow centrifugal elutriation.

Monocyte Survival Assay. Human peripheral blood monocytes progressively lose viability when cultured in absence of serum or other stimuli. Their death results from internally regulated process (apoptosis). Addition to the culture of activating factors, such as TNF-alpha

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dramatically improves cell survival and prevents DNA fragmentation. Propidium iodide (PI) staining is used to measure apoptosis as follows. Monocytes are cultured for 48 hours in polypropylene tubes in serum-free medium (positive control), in the presence of 100 ng/ml TNF-alpha (negative control), and in the presence of varying concentrations of the compound to be tested. Cells are suspended at a concentration of 2 x 10⁶/ml in PBS containing PI at a final concentration of 5 µg/ml, and then incubated at room temperature for 5 minutes before FACScan analysis. PI uptake has been demonstrated to correlate with DNA fragmentation in this experimental paradigm.

Effect on cytokine release. An important function of monocytes/macrophages is their regulatory activity on other cellular populations of the immune system through the release of cytokines after stimulation. An ELISA to measure cytokine release is performed as follows. Human monocytes are incubated at a density of 5x10⁵ cells/ml with increasing concentrations of agonists or antagonists of the invention and under the same conditions, but in the absence of agonists or antagonists. For IL-12 production, the cells are primed overnight with IFN (100 U/ml) in presence of agonist or antagonist of the invention. LPS (10 ng/ml) is then added. Conditioned media are collected after 24h and kept frozen until use. Measurement of TNF-alpha, IL-10, MCP-1 and IL-8 is then performed using a commercially available ELISA kit (e. g, R & D Systems (Minneapolis, MN)) and applying the standard protocols provided with the kit.

Oxidative burst. Purified monocytes are plated in 96-w plate at 2-1x10⁵ cell/well. Increasing concentrations of agonists or antagonists of the invention are added to the wells in a total volume of 0.2 ml culture medium (RPMI 1640 + 10% FCS, glutamine and antibiotics). After 3 days incubation, the plates are centrifuged and the medium is removed from the wells. To the macrophage monolayers, 0.2 ml per well of phenol red solution (140 mM NaCl, 10 mM potassium phosphate buffer pH 7.0, 5.5 mM dextrose, 0.56 mM phenol red and 19 U/ml of HRPO) is added, together with the stimulant (200 nM PMA). The plates are incubated at 37°C for 2 hours and the reaction is stopped by adding 20 µl 1N NaOH per well. The absorbance is read at 610 nm. To calculate the amount of H₂O₂ produced by the macrophages, a standard curve of a H₂O₂ solution of known molarity is performed for each experiment.

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The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

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Example 25: Biological Effects of Agonists or Antagonists of the Invention

Astrocyte and Neuronal Assays.

Agonists or antagonists of the invention, expressed in *Escherichia coli* and purified as described above, can be tested for activity in promoting the survival, neurite outgrowth, or phenotypic differentiation of cortical neuronal cells and for inducing the proliferation of glial fibrillary acidic protein immunopositive cells, astrocytes. The selection of cortical cells for the bioassay is based on the prevalent expression of FGF-1 and FGF-2 in cortical structures and on the previously reported enhancement of cortical neuronal survival resulting from FGF-2 treatment. A thymidine incorporation assay, for example, can be used to elucidate an agonist or antagonist of the invention's activity on these cells.

Moreover, previous reports describing the biological effects of FGF-2 (basic FGF) on cortical or hippocampal neurons in vitro have demonstrated increases in both neuron survival and neurite outgrowth (Walicke et al., "Fibroblast growth factor promotes survival of dissociated hippocampal neurons and enhances neurite extension." Proc. Natl. Acad. Sci. USA 83:3012-3016. (1986), assay herein incorporated by reference in its entirety). However, reports from experiments done on PC-12 cells suggest that these two responses are not necessarily synonymous and may depend on not only which FGF is being tested but also on which receptor(s) are expressed on the target cells. Using the primary cortical neuronal culture paradigm, the ability of an agonist or antagonist of the invention to induce neurite outgrowth can be compared to the response achieved with FGF-2 using, for example, a thymidine incorporation assay.

Fibroblast and endothelial cell assays.

Human lung fibroblasts are obtained from Clonetics (San Diego, CA) and maintained in growth media from Clonetics. Dermal microvascular endothelial cells are obtained from

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Cell Applications (San Diego, CA). For proliferation assays, the human lung fibroblasts and dermal microvascular endothelial cells can be cultured at 5,000 cells/well in a 96-well plate for one day in growth medium. The cells are then incubated for one day in 0.1% BSA basal medium. After replacing the medium with fresh 0.1% BSA medium, the cells are incubated with the test proteins for 3 days. Alamar Blue (Alamar Biosciences, Sacramento, CA) is added to each well to a final concentration of 10%. The cells are incubated for 4 hr. Cell viability is measured by reading in a CytoFluor fluorescence reader. For the PGE₂ assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or agonists or antagonists of the invention with or without IL-1α for 24 hours. The supernatants are collected and assayed for PGE₂ by EIA kit (Cayman, Ann Arbor, MI). For the IL-6 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or with or without agonists or antagonists of the invention IL-1α for 24 hours. The supernatants are collected and assayed for IL-6 by ELISA kit (Endogen, Cambridge, MA).

Human lung fibroblasts are cultured with FGF-2 or agonists or antagonists of the invention for 3 days in basal medium before the addition of Alamar Blue to assess effects on growth of the fibroblasts. FGF-2 should show a stimulation at 10 - 2500 ng/ml which can be used to compare stimulation with agonists or antagonists of the invention.

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Parkinson Models.

The loss of motor function in Parkinson's disease is attributed to a deficiency of striatal dopamine resulting from the degeneration of the nigrostriatal dopaminergic projection neurons. An animal model for Parkinson's that has been extensively characterized involves the systemic administration of 1-methyl-4 phenyl 1,2,3,6-tetrahydropyridine (MPTP). In the CNS, MPTP is taken-up by astrocytes and catabolized by monoamine oxidase B to 1-methyl-4-phenyl pyridine (MPP⁺) and released. Subsequently, MPP⁺ is actively accumulated in dopaminergic neurons by the high-affinity reuptake transporter for dopamine. MPP⁺ is then concentrated in mitochondria by the electrochemical gradient and selectively inhibits nicotidamide adenine disphosphate: ubiquinone oxidoreductionase (complex 1), thereby interfering with electron transport and eventually generating oxygen radicals.

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It has been demonstrated in tissue culture paradigms that FGF-2 (basic FGF) has trophic activity towards nigral dopaminergic neurons (Ferrari et al., Dev. Biol. 1989). Recently, Dr. Unsicker's group has demonstrated that administering FGF-2 in gel foam implants in the striatum results in the near complete protection of nigral dopaminergic neurons from the toxicity associated with MPTP exposure (Otto and Unsicker, J. Neuroscience, 1990).

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Based on the data with FGF-2, agonists or antagonists of the invention can be evaluated to determine whether it has an action similar to that of FGF-2 in enhancing dopaminergic neuronal survival in vitro and it can also be tested in vivo for protection of dopaminergic neurons in the striatum from the damage associated with MPTP treatment. The potential effect of an agonist or antagonist of the invention is first examined in vitro in a dopaminergic neuronal cell culture paradigm. The cultures are prepared by dissecting the midbrain floor plate from gestation day 14 Wistar rat embryos. The tissue is dissociated with trypsin and seeded at a density of 200,000 cells/cm² on polyorthinine-laminin coated glass coverslips. The cells are maintained in Dulbecco's Modified Eagle's medium and F12 medium containing hormonal supplements (N1). The cultures are fixed with paraformaldehyde after 8 days in vitro and are processed for tyrosine hydroxylase, a specific marker for dopminergic neurons, immunohistochemical staining. Dissociated cell cultures are prepared from embryonic rats. The culture medium is changed every third day and the factors are also added at that time.

Since the dopaminergic neurons are isolated from animals at gestation day 14, a developmental time which is past the stage when the dopaminergic precursor cells are proliferating, an increase in the number of tyrosine hydroxylase immunopositive neurons would represent an increase in the number of dopaminergic neurons surviving *in vitro*. Therefore, if an agonist or antagonist of the invention acts to prolong the survival of dopaminergic neurons, it would suggest that the agonist or antagonist may be involved in Parkinson's Disease.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

, Example 26: The Effect of Agonists or Antagonists of the Invention on the Growth of Vascular Endothelial Cells

On day 1, human umbilical vein endothelial cells (HUVEC) are seeded at 2-5x10⁴ cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin, and 50 units/ml endothelial cell growth supplements (ECGS, Biotechnique, Inc.). On day 2, the medium is replaced with M199 containing 10% FBS, 8 units/ml heparin. An agonist or antagonist of the invention, and positive controls, such as VEGF and basic FGF (bFGF) are added, at varying concentrations. On days 4 and 6, the medium is replaced. On day 8, cell number is determined with a Coulter Counter.

An increase in the number of HUVEC cells indicates that the compound of the invention may proliferate vascular endothelial cells, while a decrease in the number of HUVEC cell indicates that the compound of the invention inhibits vascular endothelial cells.

The studies described in this example tested activity of a polypeptide of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), agonists, and/or antagonists of the invention.

Example 27: Rat Corneal Wound Healing Model

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- This animal model shows the effect of an agonist or antagonist of the invention on an envascularization. The experimental protocol includes:
- a) Making a 1-1.5 mm long incision from the center of comea into the stromal layer.
- b) Inserting a spatula below the lip of the incision facing the outer corner of the
 25 eye.
 - c) Making a pocket (its base is 1-1.5 mm form the edge of the eye).
 - d) Positioning a pellet, containing 50ng- 5ug of an agonist or antagonist of the invention, within the pocket.
- e) Treatment with an agonist or antagonist of the invention can also be applied
 30 topically to the corneal wounds in a dosage range of 20mg 500mg (daily treatment for five days).

The studies described in this example tested activity of agonists or antagonists of the

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invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 28: Diabetic Mouse and Glucocorticoid-Impaired Wound Healing Models

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A. Diabetic db+/db+ Mouse Model.

To demonstrate that an agonist or antagonist of the invention accelerates the healing process, the genetically diabetic mouse model of wound healing is used. The full thickness wound healing model in the db+/db+ mouse is a well characterized, clinically relevant and reproducible model of impaired wound healing. Healing of the diabetic wound is dependent on formation of granulation tissue and re-epithelialization rather than contraction (Gartner, M.H. et al., J. Surg. Res. 52:389 (1992); Greenhalgh, D.G. et al., Am. J. Pathol. 136:1235 (1990)).

The diabetic animals have many of the characteristic features observed in Type II diabetes mellitus. Homozygous (db+/db+) mice are obese in comparison to their normal heterozygous (db+/+m) littermates. Mutant diabetic (db+/db+) mice have a single autosomal recessive mutation on chromosome 4 (db+) (Coleman et al. Proc. Natl. Acad. Sci. USA 77:283-293 (1982)). Animals show polyphagia, polydipsia and polyuria. Mutant diabetic mice (db+/db+) have elevated blood glucose, increased or normal insulin levels, and suppressed cell-mediated immunity (Mandel et al., J. Immunol. 120:1375 (1978); Debray-Sachs, M. et al., Clin. Exp. Immunol. 51(1):1-7 (1983); Leiter et al., Am. J. of Pathol. 114:46-55 (1985)). Peripheral neuropathy, myocardial complications, and microvascular lesions, basement membrane thickening and glomerular filtration abnormalities have been described in these animals (Norido, F. et al., Exp. Neurol. 83(2):221-232 (1984); Robertson et al., Diabetes 29(1):60-67 (1980); Giacomelli et al., Lab Invest. 40(4):460-473 (1979); Coleman, D.L., Diabetes 31 (Suppl):1-6 (1982)). These homozygous diabetic mice develop hyperglycemia that is resistant to insulin analogous to human type II diabetes (Mandel et al., J. Immunol. 120:1375-1377 (1978)).

The characteristics observed in these animals suggests that healing in this model may be similar to the healing observed in human diabetes (Greenhalgh, et al., Am. J. of Pathol. 136:1235-1246 (1990)).

Genetically diabetic female C57BL/KsJ (db+/db+) mice and their non-diabetic

(db+/+m) heterozygous littermates are used in this study (Jackson Laboratories). The animals are purchased at 6 weeks of age and are 8 weeks old at the beginning of the study. Animals are individually housed and received food and water ad libitum. All manipulations are performed using aseptic techniques. The experiments are conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

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Wounding protocol is performed according to previously reported methods (Tsuboi, R. and Rifkin, D.B., J. Exp. Med. 172:245-251 (1990)). Briefly, on the day of wounding, animals are anesthetized with an intraperitoneal injection of Avertin (0.01 mg/mL), 2,2,2-tribromoethanol and 2-methyl-2-butanol dissolved in deionized water. The dorsal region of the animal is shaved and the skin washed with 70% ethanol solution and iodine. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is then created using a Keyes tissue punch. Immediately following wounding, the surrounding skin is gently stretched to eliminate wound expansion. The wounds are left open for the duration of the experiment. Application of the treatment is given topically for 5 consecutive days commencing on the day of wounding. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of surgery and at two day intervals thereafter. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

An agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology and immunohistochemistry. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

Three groups of 10 animals each (5 diabetic and 5 non-diabetic controls) are evaluated: 1)

Vehicle placebo control, 2) untreated group, and 3) treated group.

Wound closure is analyzed by measuring the area in the vertical and horizontal axis and

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obtaining the total square area of the wound. Contraction is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

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[Open area on day 8] - [Open area on day 1] / [Open area on day 1]

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using a Reichert-Jung microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds are used to assess whether the healing process and the morphologic appearance of the repaired skin is altered by treatment with an agonist or antagonist of the invention. This assessment included verification of the presence of cell accumulation, inflammatory cells, capillaries, fibroblasts, re-epithelialization and epidermal maturity (Greenhalgh, D.G. et al., Am. J. Pathol. 136:1235 (1990)). A calibrated lens micrometer is used by a blinded observer.

Tissue sections are also stained immunohistochemically with a polyclonal rabbit antihuman keratin antibody using ABC Elite detection system. Human skin is used as a positive tissue control while non-immune IgG is used as a negative control. Keratinocyte growth is determined by evaluating the extent of reepithelialization of the wound using a calibrated lens micrometer.

Proliferating cell nuclear antigen/cyclin (PCNA) in skin specimens is demonstrated by using anti-PCNA antibody (1:50) with an ABC Elite detection system. Human colon cancer served as a positive tissue control and human brain tissue is used as a negative tissue control. Each specimen included a section with omission of the primary antibody and substitution with non-immune mouse IgG. Ranking of these sections is based on the extent of proliferation on a scale of 0-8, the lower side of the scale reflecting slight proliferation to the higher side reflecting intense proliferation.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

B. Steroid Impaired Rat Model

The inhibition of wound healing by steroids has been well documented in various in vitro and in vivo systems (Wahl, Glucocorticoids and Wound healing. In: Anti-Inflammatory Steroid Action: Basic and Clinical Aspects. 280-302 (1989); Wahlet al., J. Immunol. 115: 476-481 (1975); Werb et al., J. Exp. Med. 147:1684-1694 (1978)). Glucocorticoids retard wound healing by inhibiting angiogenesis, decreasing vascular permeability (Ebert et al., An. Intern. Med. 37:701-705 (1952)), fibroblast proliferation, and collagen synthesis (Beck et al., Growth Factors. 5: 295-304 (1991); Haynes et al., J. Clin. Invest. 61: 703-797 (1978)) and producing a transient reduction of circulating monocytes (Haynes et al., J. Clin. Invest. 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid 10 Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989)). The systemic administration of steroids to impaired wound healing is a well establish phenomenon in rats (Beck et al., Growth Factors. 5: 295-304 (1991); Haynes et al., J. Clin. Invest. 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989); Pierce et al., Proc. Natl. Acad. Sci. USA 86: 2229-2233 (1989)).

To demonstrate that an agonist or antagonist of the invention can accelerate the healing process, the effects of multiple topical applications of the agonist or antagonist on full thickness excisional skin wounds in rats in which healing has been impaired by the systemic administration of methylprednisolone is assessed.

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Young adult male Sprague Dawley rats weighing 250-300 g (Charles River Laboratories) are used in this example. The animals are purchased at 8 weeks of age and are 9 weeks old at the beginning of the study. The healing response of rats is impaired by the systemic administration of methylprednisolone (17mg/kg/rat intramuscularly) at the time of wounding. Animals are individually housed and received food and water ad libitum. All manipulations are performed using aseptic techniques. This study is conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

The wounding protocol is followed according to section A, above. On the day of wounding, animals are anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (5 mg/kg). The dorsal region of the animal is shaved and the skin washed with 70% ethanol and iodine solutions. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is created using a Keyes tissue punch. The

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wounds are left open for the duration of the experiment. Applications of the testing materials are given topically once a day for 7 consecutive days commencing on the day of wounding and subsequent to methylprednisolone administration. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of wounding and at the end of treatment. Wound closure is determined by daily measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

The agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for histology. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

Four groups of 10 animals each (5 with methylprednisolone and 5 without glucocorticoid) are evaluated: 1) Untreated group 2) Vehicle placebo control 3) treated groups.

Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total area of the wound. Closure is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

[Open area on day 8] - [Open area on day 1] / [Open area on day 1]

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using an Olympus microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds allows assessment of whether the healing process and the morphologic appearance of the repaired skin is improved by treatment with an agonist or

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antagonist of the invention. A calibrated lens micrometer is used by a blinded observer to determine the distance of the wound gap.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polyneptides of the invention (e.g., gene therapy).

Example 29: Lymphadema Animal Model

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The purpose of this experimental approach is to create an appropriate and consistent lymphedema model for testing the therapeutic effects of an agonist or antagonist of the invention in lymphangiogenesis and re-establishment of the lymphatic circulatory system in the rat hind limb. Effectiveness is measured by swelling volume of the affected limb, quantification of the amount of lymphatic vasculature, total blood plasma protein, and histopathology. Acute lymphedema is observed for 7-10 days. Perhaps more importantly, the chronic progress of the edema is followed for up to 3-4 weeks.

Prior to beginning surgery, blood sample is drawn for protein concentration analysis. Male rats weighing approximately ~350g are dosed with Pentobarbital. Subsequently, the right legs are shaved from knee to hip. The shaved area is swabbed with gauze soaked in 70% EtOH. Blood is drawn for serum total protein testing. Circumference and volumetric measurements are made prior to injecting dye into paws after marking 2 measurement levels (0.5 cm above heel, at mid-pt of dorsal paw). The intradermal dorsum of both right and left paws are injected with 0.05 ml of 1% Evan's Blue. Circumference and volumetric measurements are then made following injection of dye into paws.

Using the knee joint as a landmark, a mid-leg inguinal incision is made circumferentially allowing the femoral vessels to be located. Forceps and hemostats are used to dissect and separate the skin flaps. After locating the femoral vessels, the lymphatic vessel that runs along side and underneath the vessel(s) is located. The main lymphatic vessels in this area are then electrically coagulated or suture ligated.

Using a microscope, muscles in back of the leg (near the semitendinosis and adductors) are bluntly dissected. The popliteal lymph node is then located. The 2 proximal

and 2 distal lymphatic vessels and distal blood supply of the popliteal node are then and ligated by suturing. The popliteal lymph node, and any accompanying adipose tissue, is then removed by cutting connective tissues.

Care is taken to control any mild bleeding resulting from this procedure. After lymphatics are occluded, the skin flaps are sealed by using liquid skin (Vetbond) (AJ Buck). The separated skin edges are sealed to the underlying muscle tissue while leaving a gap of ~0.5 cm around the leg. Skin also may be anchored by suturing to underlying muscle when necessary.

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To avoid infection, animals are housed individually with mesh (no bedding). Recovering animals are checked daily through the optimal edematous peak, which typically occurred by day 5-7. The plateau edematous peak are then observed. To evaluate the intensity of the lymphedema, the circumference and volumes of 2 designated places on each paw before operation and daily for 7 days are measured. The effect plasma proteins on lymphedema is determined and whether protein analysis is a useful testing perimeter is also investigated. The weights of both control and edematous limbs are evaluated at 2 places. Analysis is performed in a blind manner.

Circumference Measurements: Under brief gas anesthetic to prevent limb movement, a cloth tape is used to measure limb circumference. Measurements are done at the ankle bone and dorsal paw by 2 different people then those 2 readings are averaged. Readings are taken from both control and edematous limbs.

Volumetric Measurements: On the day of surgery, animals are anesthetized with Pentobarbital and are tested prior to surgery. For daily volumetrics animals are under brief halothane anesthetic (rapid immobilization and quick recovery), both legs are shaved and equally marked using waterproof marker on legs. Legs are first dipped in water, then dipped into instrument to each marked level then measured by Buxco edema software(Chen/Victor). Data is recorded by one person, while the other is dipping the limb to marked area.

Blood-plasma protein measurements: Blood is drawn, spun, and serum separated prior to surgery and then at conclusion for total protein and Ca2+ comparison.

Limb Weight Comparison: After drawing blood, the animal is prepared for tissue collection. The limbs are amputated using a quillitine, then both experimental and control legs are cut at the ligature and weighed. A second weighing is done as the tibio-cacaneal joint is disarticulated and the foot is weighed.

Histological Preparations: The transverse muscle located behind the knee (popliteal) area is dissected and arranged in a metal mold, filled with freezeGel, dipped into cold methylbutane, placed into labeled sample bags at - 80EC until sectioning. Upon sectioning, the muscle is observed under fluorescent microscopy for lymphatics..

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 30: Suppression of TNF alpha-induced adhesion molecule expression by a Agonist or Antagonist of the Invention

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The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Tumor necrosis factor alpha (TNF-a), a potent proinflammatory cytokine, is a stimulator of all three CAMs on endothelial cells and may be involved in a wide variety of inflammatory responses, often resulting in a pathological outcome.

The potential of an agonist or antagonist of the invention to mediate a suppression of TNF-a induced CAM expression can be examined. A modified ELISA assay which uses ECs as a solid phase absorbent is employed to measure the amount of CAM expression on TNF-a treated ECs when co-stimulated with a member of the FGF family of proteins.

To perform the experiment, human umbilical vein endothelial cell (HUVEC) cultures are obtained from pooled cord harvests and maintained in growth medium (EGM-2; Clonetics, San Diego, CA) supplemented with 10% FCS and 1% penicillin/streptomycin in a 37 degree C humidified incubator containing 5% CO₂. HUVECs are seeded in 96-well

plates at concentrations of 1 x 10⁴ cells/well in EGM medium at 37 degree C for 18-24 hrs or until confluent. The monolayers are subsequently washed 3 times with a serum-free solution of RPMI-1640 supplemented with 100 U/ml penicillin and 100 mg/ml streptomycin, and treated with a given cytokine and/or growth factor(s) for 24 h at 37 degree C. Following incubation, the cells are then evaluated for CAM expression.

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Human Umbilical Vein Endothelial cells (HUVECs) are grown in a standard 96 well plate to confluence. Growth medium is removed from the cells and replaced with 90 ul of 199 Medium (10% FBS). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 ul volumes). Plates are incubated at 37 degree C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 µl of 0.1% paraformaldehyde-PBS(with Ca++ and Mg++) is added to each well. Plates are held at 4°C for 30 min.

Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. Add 10 μl of diluted primary antibody to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 μg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA.

Then add 20 μ l of diluted ExtrAvidin-Alkaline Phosphotase (1:5,000 dilution) to each well and incubated at 37°C for 30 min. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 ml of glycine buffer (pH 10.4). 100 μ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphotase in glycine buffer: 1:5,000 (10^{0}) > $10^{-0.5}$ > 10^{-1} > $10^{-1.5}$.5 μ l of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 μ l of pNNP reagent must then be added to each of the standard wells. The plate must be incubated at 37°C for 4h. A volume of 50 μ l of 3M NaOH is added to all wells. The results are quantified on a plate reader at 405 nm. The background subtraction option is used on blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

The studies described in this example tested activity of agonists or antagonists of the

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invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 31: Production Of Polypeptide of the Invention For High-Throughput Screening
Assays

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The following protocol produces a supernatant containing polypeptide of the present invention to be tested. This supernatant can then be used in the Screening Assays described in Examples 33-42.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2 x 10⁵ cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in Examples 8-10, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on

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PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37 degree C for 6 hours.

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While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or HGS CHO-5 media (116.6 mg/L of CaCl2 (anhyd); 0.00130 mg/L CuSO₄-5H₂O; 0.050 mg/L of Fe(NO₃)₃-9H₂O; 0.417 mg/L of FeSO₄-7H₂O; 311.80 mg/L of Kcl; 28.64 mg/L of MgCl₂; 48.84 mg/L of MgSO₄; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO3; 62.50 mg/L of NaH2PO4-H20; 71.02 mg/L of Na2HPO4; .4320 mg/L of ZnSO4-7H2O; .002 mg/L of Arachidonic Acid; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine-H₂0; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL-H₂0; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H₂0; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalainine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tryrosine-2Na-2H20; and 99.65 mg/ml of L-Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 25 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; 0.680 mg/L of Vitamin B₁₂; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite: 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal Acetate. Adjust

osmolarity to 327 mOsm) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37 degree C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 33-40.

It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide of the present invention directly (e.g., as a secreted protein) or by polypeptide of the present invention inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

Example 32: Construction of GAS Reporter Construct

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One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon

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tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

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The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:1686)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

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			<u>JAKs</u>		STATS GAS(elements) or ISRE		
	Ligand	tyk2	<u>Jak l</u>	<u>Jak2</u>	Jak3		
	IFM County						
_	IFN family						ICDE
5	IFN-a/B	+	+	•	-	1,2,3	ISRE
	IFN-g		+	+	•	ł	GAS
	(IRFi>Lys6>IFP)		_				
	II-10	+	?	?	•	1,3	
10	gp130 family				_		
	IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS
	(IRF1>Lys6>IFP)						
	II-11(Pleiotrohic)	?	+	?	?	1,3	
	OnM(Pleiotrohic)	?	+	+	?	1,3	
15	LIF(Pleiotrohic)	?	+	+	?	1,3	
	CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
	G-CSF(Pleiotrohic)	?	+	?	?	1,3	
	IL-12(Pleiotrohic)	+	-	+	+	1,3	
	0.0						
20	g-C family						
	IL-2 (lymphocytes)	•	+	-	+	1,3,5	GAS
	IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP)
	>>Ly6)(IgH)	•				,	
	IL-7 (lymphocytes)	-	+	-	+	5	GAS
25	IL-9 (lymphocytes)	-	+	-	+	5	GAS
	IL-13 (lymphocyte)	-	+	?	?	6	GAS
	IL-15	?	+	?	+	5	GAS
	gp140 family						
30						5	GAS
<i>3</i> 0	IL-3 (myeloid)	•	-	+	-	J	GAS
	(IRF1>IFP>>Ly6)						CAS
	IL-5 (myeloid)	-	-	+	-	5	GAS
	GM-CSF (myeloid)	•	-	+	-	5	GAS

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	Growth hormone fami	<u>ly</u>					
	GH	?	-	+	-	5	
	PRL	?	+/-	+	-	1,3,5	
5	EPO	?	-	+	-	5	GAS(B-
	CAS>IRF1=IFP>>Lyc	5)			•		
	Receptor Tyrosine Kin	ases					
	EGF	?	+	+	-	1,3	GAS (IRF1)
10							
	PDGF	?	+	+	, -	1,3	
	CSF-1	?	+	+	-	1,3	GAS (not IRF1)

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 33-34, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

10 5':GCGCCTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAATGATTTCCCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:1687)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:1688)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with Xhol/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

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5':CTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAA TGATTTCCCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCG CCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCT CCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCC TCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTTGGAGGCCTA 25 GGCTTTTGCAAAAAGCTT:3' (SEQ ID NO:1689)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol

acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindlII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using Sall and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 33-34.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 35 and 36. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, Il-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

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Example 33: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, and determining whether supernate containing a polypeptide of the invention proliferates and/or differentiates T-cells. T-cell activity is assessed using the

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GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml genticin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies) with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10⁷ per transfection), and resuspend in OPTI-MEM to a final concentration of 10⁷ cells/ml. Then add 1ml of 1 x 10⁷ cells in OPTI-MEM to T25 flask and incubate at 37 degree C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing polypeptide of the present invention or polypeptide of the present invention induced polypeptides as produced by the protocol described in Example 31.

On the day of treatment with the supernatant, the cells should be washed and

resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

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After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20 degree C until SEAP assays are performed according to Example 37. The plates containing the remaining treated cells are placed at 4 degree C and serve as a source of material for repeating the assay on a specific well if desired.

As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

The above protocol may be used in the generation of both transient, as well as, stable transfected cells, which would be apparent to those of skill in the art.

Example 34: High-Throughput Screening Assay Identifying Myeloid Activity

The following protocol is used to assess myeloid activity of polypeptide of the present invention by determining whether polypeptide of the present invention proliferates and/or differentiates myeloid cells. Myeloid cell activity is assessed using

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the GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 32, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2x10e⁷ U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM Na₂HPO₄.7H₂O, 1 mM MgCl₂, and 675 uM CaCl₂. Incubate at 37 degrees C for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37 degree C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting $1x10^8$ cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of $5x10^5$ cells/ml. Plate 200 ul cells per well in the 96-well plate (or $1x10^5$ cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 31. Incubate at 37 degee C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 37.

30 Example 35: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed by polypeptide of the present invention.

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Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells by polypeptide of the present invention can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

- 5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO: 1690)
 - 5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO 1691)

Using the GAS:SEAP/Neo vector produced in Example 32, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter

sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 31. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as 5×10^5 cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1×10^5 cells/well). Add 50 ul supernatant produced by Example 31, 37 degree C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 37.

Example 36: High-Throughput Screening Assay for T-cell Activity

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NF-KB (Nuclear Factor KB) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-KB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- KB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

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In non-stimulated conditions, NF- KB is retained in the cytoplasm with I-KB (Inhibitor KB). However, upon stimulation, I- KB is phosphorylated and degraded, causing NF- KB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- KB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-KB promoter element are used to screen the supernatants produced in Example 31. Activators or inhibitors of NF-KB would be useful in treating, preventing, and/or diagnosing diseases. For example, inhibitors of NF-KB could be used to treat those diseases related to the acute or chronic activation of NF-KB, such as rheumatoid arthritis.

To construct a vector containing the NF-KB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-KB binding site (GGGGACTTTCCC) (SEQ ID NO:1692), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an Xhol site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGAC
TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:1693)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:1688)

PCR amplification is performed using the SV40 promoter template present in 30 the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is

digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGACTTTCC
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCC
ATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGA
CTAATTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTA
TTCCAGAAGTAGTGAGGAGGCCTTTTTTTGGAGGCCTAGGCTTTTTGCAAAAA
GCTT:3' (SEQ ID NO:1694)

Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-KB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF-KB/SV40/SEAP cassette is removed from the above NF-KB/SEAP vector using restriction enzymes Sall and Notl, and inserted into a vector containing neomycin resistance. Particularly, the NF-KB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with Sall and Notl.

Once NF-KB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 33. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 33. As a positive control, exogenous TNF alpha (0.1,1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

25 Example 37: Assay for SEAP Activity

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As a reporter molecule for the assays described in Examples 33-36, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 ul of 2.5x dilution buffer into Optiplates containing 35 ul of a supernatant. Seal the plates with a plastic sealer and incubate at 65 degree C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 ml Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 ul Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

15 Reaction Buffer Formulation:

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# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6

23	125	6.25
24	130	6.5
25	135	6.75
26	140	7
27	145	7.25
28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32 .	.170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

Example 38: High-Throughput Screening Assay Identifying Changes in Small

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Molecule Concentration and Membrane Permeability

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Binding of a ligand to a receptor is known to alter intracellular levels of small molecules. such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4, 50 ul of 12 ug/ml fluo-4 is added to each well. The plate is incubated at 37 degrees C in a CO₂ incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10⁶ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37 degrees C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10⁶ cells/ml, and dispensed into a microplate. 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley Cell Wash with 200 ul, followed by an aspiration step to 100 ul final volume.

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For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-4. The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event caused by the a molecule, either polypeptide of the present invention or a molecule induced by polypeptide of the present invention, which has resulted in an increase in the intracellular Ca⁺⁺ concentration.

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Example 40: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, identifying whether polypeptide of the present invention or a molecule induced by polypeptide of the present invention is capable of activating tyrosine

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kinase signal transduction pathways is of interest. Therefore, the following protocol is designed to identify such molecules capable of activating the tyrosine kinase signal transduction pathways.

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Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford,MA), or calf serum, rinsed with PBS and stored at 4 degree C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford,MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 31, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na3VO4, 2 mM Na4P2O7 and a cocktail of protease inhibitors (# 1836170) obtained from Boeheringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after

detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4 degree C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

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Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂₊ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30 degree C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mm EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37 degree C for 20 min. This allows the streptavadin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phospotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37 degree C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound

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peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

Example 41: High-Throughput Screening Assay Identifying Phosphorylation Activity

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As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 40, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), 1RAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

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Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (lug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4 degree C until use.

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A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 31 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

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After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit)

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antibody (lug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation by polypeptide of the present invention or a molecule induced by polypeptide of the present invention.

Example 42: Assay for the Stimulation of Bone Marrow CD34+ Cell Proliferation

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This assay is based on the ability of human CD34+ to proliferate in the presence of hematopoietic growth factors and evaluates the ability of isolated polypeptides expressed in mammalian cells to stimulate proliferation of CD34+ cells.

It has been previously shown that most mature precursors will respond to only a single signal. More immature precursors require at least two signals to respond. Therefore, to test the effect of polypeptides on hematopoietic activity of a wide range of progenitor cells, the assay contains a given polypeptide in the presence or absence of other hematopoietic growth factors. Isolated cells are cultured for 5 days in the presence of Stem Cell Factor (SCF) in combination with tested sample. SCF alone has a very limited effect on the proliferation of bone marrow (BM) cells, acting in such conditions only as a "survival" factor. However, combined with any factor exhibiting stimulatory effect on these cells (e.g., IL-3), SCF will cause a synergistic effect. Therefore, if the tested polypeptide has a stimulatory effect on a hematopoietic progenitors, such activity can be easily detected. Since normal BM cells have a low level of cycling cells, it is likely that any inhibitory effect of a given polypeptide, or agonists or antagonists thereof, might not be detected. Accordingly, assays for an inhibitory effect on progenitors is preferably tested in cells that are first subjected to in vitro stimulation with SCF+IL+3, and then contacted with the compound that is being evaluated for inhibition of such induced proliferation.

Briefly, CD34+ cells are isolated using methods known in the art. The cells

are thawed and resuspended in medium (QBSF 60 serum-free medium with 1% L-glutamine (500ml) Quality Biological, Inc., Gaithersburg, MD Cat# 160-204-101). After several gentle centrifugation steps at 200 x g, cells are allowed to rest for one hour. The cell count is adjusted to 2.5×10^5 cells/ml. During this time, $100 \mu l$ of sterile water is added to the peripheral wells of a 96-well plate. The cytokines that can be tested with a given polypeptide in this assay is rhSCF (R&D Systems, Minneapolis, MN, Cat# 255-SC) at 50 ng/ml alone and in combination with rhSCF and rhIL-3 (R&D Systems, Minneapolis, MN, Cat# 203-ML) at 30 ng/ml. After one hour, $10 \mu l$ of prepared cytokines, $50 \mu l$ of the supernatants prepared in Example 31 (supernatants at 1:2 dilution = $50 \mu l$) and $20 \mu l$ of diluted cells are added to the media which is already present in the wells to allow for a final total volume of $100 \mu l$. The plates are then placed in a 37° C/5% CO₂ incubator for five days.

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Eighteen hours before the assay is harvested, 0.5 μ Ci/well of [3H] Thymidine is added in a 10 μ l volume to each well to determine the proliferation rate. The experiment is terminated by harvesting the cells from each 96-well plate to a filtermat using the Tomtec Harvester 96. After harvesting, the filtermats are dried, trimmed and placed into OmniFilter assemblies consisting of one OmniFilter plate and one OmniFilter Tray. 60 μ l Microscint is added to each well and the plate sealed with TopSeal-A press-on sealing film A bar code 15 sticker is affixed to the first plate for counting. The sealed plates is then loaded and the level of radioactivity determined via the Packard Top Count and the printed data collected for analysis. The level of radioactivity reflects the amount of cell proliferation.

The studies described in this example test the activity of a given polypeptide to stimulate bone marrow CD34+ cell proliferation. One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof. As a nonlimiting example, potential antagonists tested in this assay would be expected to inhibit cell proliferation in the presence of cytokines and/or to increase the inhibition of cell proliferation in the presence of cytokines and a given polypeptide. In contrast, potential agonists tested in this assay would be expected to enhance cell

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proliferation and/or to decrease the inhibition of cell proliferation in the presence of cytokines and a given polypeptide.

The ability of a gene to stimulate the proliferation of bone marrow CD34+ cells indicates that polynucleotides and polypeptides corresponding to the gene are useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein.

Example 43: Assay for Extracellular Matrix Enhanced Cell Response (EMECR)

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The objective of the Extracellular Matrix Enhanced Cell Response (EMECR) assay is to identify gene products (e.g., isolated polypeptides) that act on the hematopoietic stem cells in the context of the extracellular matrix (ECM) induced signal.

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Cells respond to the regulatory factors in the context of signal(s) received from the surrounding microenvironment. For example, fibroblasts, and endothelial and epithelial stem cells fail to replicate in the absence of signals from the ECM. Hematopoietic stem cells can undergo self-renewal in the bone marrow, but not in *in vitro* suspension culture. The ability of stem cells to undergo self-renewal *in vitro* is dependent upon their interaction with the stromal cells and the ECM protein fibronectin (fn). Adhesion of cells to fn is mediated by the $\alpha_5.\beta_1$ and $\alpha_4.\beta_1$ integrin receptors, which are expressed by human and mouse hematopoietic stem cells. The factor(s) which integrate with the ECM environment and responsible for stimulating stem cell self-renewal has not yet been identified. Discovery of such factors should be of great interest in gene therapy and bone marrow transplant applications

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Briefly, polystyrene, non tissue culture treated, 96-well plates are coated with fn fragment at a coating concentration of $0.2 \,\mu\text{g/cm}^2$. Mouse bone marrow cells are plated (1,000 cells/well) in 0.2 ml of serum-free medium. Cells cultured in the presence of IL-3 (5 ng/ml) + SCF (50 ng/ml) would serve as the positive control,

conditions under which little self-renewal but pronounced differentiation of the stem cells is to be expected. Gene products of the invention (e.g., including, but not limited to, polynucleotides and polypeptides of the present invention, and supernatants produced in Example 31), are tested with appropriate negative controls in the presence and absence of SCF(5.0 ng/ml), where test factor supernates represent 10% of the total assay volume. The plated cells are then allowed to grow by incubating in a low oxygen environment (5% CO₂, 7% O₂, and 88% N₂) tissue culture incubator for 7 days. The number of proliferating cells within the wells is then quantitated by measuring thymidine incorporation into cellular DNA. Verification of the positive hits in the assay will require phenotypic characterization of the cells, which can be accomplished by scaling up of the culture system and using appropriate antibody reagents against cell surface antigens and FACScan.

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One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

If a particular polypeptide of the present invention is found to be a stimulator of hematopoietic progenitors, polynucleotides and polypeptides corresponding to the gene encoding said polypeptide may be useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein. The gene product may also be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Additionally, the polynucleotides and/or polypeptides of the gene of interest and/or agonists and/or antagonists thereof, may also be employed to inhibit the proliferation and differentiation of hematopoietic cells and therefore may be employed to protect bone marrow stem cells from chemotherapeutic agents during chemotherapy. This antiproliferative effect may allow administration of higher doses of chemotherapeutic agents and, therefore, more effective chemotherapeutic treatment.

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Moreover, polynucleotides and polypeptides corresponding to the gene of interest may also be useful for the treatment and diagnosis of hematopoietic related disorders such as, for example, anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex-vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

Example 44: Human Dermal Fibroblast and Aortic Smooth Muscle Cell Proliferation

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The polypeptide of interest is added to cultures of normal human dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AoSMC) and two coassays are performed with each sample. The first assay examines the effect of the polypeptide of interest on the proliferation of normal human dermal fibroblasts (NHDF) or aortic smooth muscle cells (AoSMC). Aberrant growth of fibroblasts or smooth muscle cells is a part of several pathological processes, including fibrosis, and restenosis. The second assay examines IL6 production by both NHDF and SMC. IL6 production is an indication of functional activation. Activated cells will have increased production of a number of cytokines and other factors, which can result in a proinflammatory or immunomodulatory outcome. Assays are run with and without co-TNFa stimulation, in order to check for costimulatory or inhibitory activity.

Briefly, on day 1, 96-well black plates are set up with 1000 cells/well (NHDF) or 2000 cells/well (AoSMC) in 100 μl culture media. NHDF culture media contains: Clonetics FB basal media, 1mg/ml hFGF, 5mg/ml insulin, 50mg/ml gentamycin, 2%FBS, while AoSMC culture media contains Clonetics SM basal media, 0.5 μg/ml hEGF, 5mg/ml insulin, 1μg/ml hFGF, 50mg/ml gentamycin, 50 μg/ml Amphotericin B, 5%FBS. After incubation at 37°C for at least 4-5 hours, culture media is aspirated and replaced with growth arrest media. Growth arrest media for NHDF contains fibroblast basal media, 50mg/ml gentamycin, 2% FBS, while growth arrest media for AoSMC contains SM basal media, 50mg/ml gentamycin, 50μg/ml Amphotericin B,

0.4% FBS. Incubate at 37°C until day 2.

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On day 2, serial dilutions and templates of the polypeptide of interest are designed such that they always include media controls and known-protein controls. For both stimulation and inhibition experiments, proteins are diluted in growth arrest media. For inhibition experiments, TNFa is added to a final concentration of 2ng/ml (NHDF) or 5ng/ml (AoSMC). Add 1/3 vol media containing controls or polypeptides of the present invention and incubate at 37°C/5% CO₂ until day 5.

Transfer 60µl from each well to another labeled 96-well plate, cover with a plate-sealer, and store at 4°C until Day 6 (for IL6 ELISA). To the remaining 100 µl in the cell culture plate, aseptically add Alamar Blue in an amount equal to 10% of the culture volume (10µl). Return plates to incubator for 3 to 4 hours. Then measure fluorescence with excitation at 530nm and emission at 590nm using the CytoFluor. This yields the growth stimulation/inhibition data.

On day 5, the IL6 ELISA is performed by coating a 96 well plate with 50-100 ul/well of Anti-Human IL6 Monoclonal antibody diluted in PBS, pH 7.4, incubate ON at room temperature.

On day 6, empty the plates into the sink and blot on paper towels. Prepare Assay Buffer containing PBS with 4% BSA. Block the plates with 200 µl/well of Pierce Super Block blocking buffer in PBS for 1-2 hr and then wash plates with wash buffer (PBS, 0.05% Tween-20). Blot plates on paper towels. Then add 50 µl/well of diluted Anti-Human IL-6 Monoclonal, Biotin-labeled antibody at 0.50 mg/ml. Make dilutions of IL-6 stock in media (30, 10, 3, 1, 0.3, 0 ng/ml). Add duplicate samples to top row of plate. Cover the plates and incubate for 2 hours at RT on shaker. Plates are washed with wash buffer and blotted on paper towels. Dilute EU-labeled Streptavidin 1:1000 in Assay buffer, and add 100 µl/well. Cover the plate and incubate 1 h at RT. Plates are again washed with wash buffer and blotted on paper towels. Add 100 µl/well of Enhancement Solution and shake for 5 minutes. Read the plate on the Wallac DELFIA Fluorometer. Readings from triplicate samples in each assay are tabulated and averaged.

A positive result in this assay suggests AoSMC cell proliferation and that the

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polypeptide of the present invention may be involved in dermal fibroblast proliferation and/or smooth muscle cell proliferation. A positive result also suggests many potential uses of polypeptides, polynucleotides, agonists and/or antagonists of the polynucleotide/polypeptide of the present invention which gives a positive result. For example, inflammation and immune responses, wound healing, and angiogenesis, as detailed throughout this specification. Particularly, polypeptides of the present invention and polynucleotides of the present invention may be used in wound healing and dermal regeneration, as well as the promotion of vasculargenesis, both of the blood vessels and lymphatics. The growth of vessels can be used in the treatment of. for example, cardiovascular diseases. Additionally, antagonists of polypeptides and polynucleotides of the invention may be useful in treating diseases, disorders, and/or conditions which involve angiogenesis by acting as an anti-vascular (e.g., antiangiogenesis). These diseases, disorders, and/or conditions are known in the art and/or are described herein, such as, for example, malignancies, solid tumors, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; artheroscleric plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, comeal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uvietis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis. Moreover, antagonists of polypeptides and polynucleotides of the invention may be useful in treating anti-hyperproliferative diseases and/or anti-inflammatory known in the art and/or described herein.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or

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antagonists and fragments and variants thereof.

Example 45: Cellular Adhesion Molecule (CAM) Expression on Endothelial Cells

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The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Briefly, endothelial cells (e.g., Human Umbilical Vein Endothelial cells (HUVECs)) are grown in a standard 96 well plate to confluence, growth medium is removed from the cells and replaced with 100 μl of 199 Medium (10% fetal bovine serum (FBS)). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 μl volumes). Plates are then incubated at 37°C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 μl of 0.1% paraformaldehyde-PBS(with Ca++ and Mg++) is added to each well. Plates are held at 4°C for 30 min. Fixative is removed from the wells and wells are washed 1X with PBS(+Ca,Mg) + 0.5% BSA and drained. 10 μl of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 μg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed three times with PBS(+Ca,Mg) + 0.5% BSA. 20 μl of diluted ExtrAvidin-Alkaline

Phosphotase (1:5,000 dilution, refered to herein as the working dilution) are added to each well and incubated at 37°C for 30 min. Wells are washed three times with PBS(+Ca,Mg)+0.5% BSA. Dissolve I tablet of p-Nitrophenol Phosphate pNPP per 5 ml of glycine buffer (pH 10.4). 100 μ l of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphotase in glycine buffer: 1:5,000 (10°) > 10^{-0.5} > 10⁻¹ > 10^{-1.5}. 5 μ l of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 μ l of pNNP reagent is then added to each of the standard wells. The plate is incubated at 37°C for 4h. A volume of 50 μ l of 3M NaOH is added to all wells. The plate is read on a plate reader at 405 nm using the background subtraction option on blank wells filled with glycine buffer only. Additionally, the template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

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Example 46: Alamar Blue Endothelial Cells Proliferation Assay

This assay may be used to quantitatively determine protein mediated inhibition of bFGF-induced proliferation of Bovine Lymphatic Endothelial Cells (LECs), Bovine Aortic Endothelial Cells (BAECs) or Human Microvascular Uterine Myometrial Cells (UTMECs). This assay incorporates a fluorometric growth indicator based on detection of metabolic activity. A standard Alamar Blue Proliferation Assay is prepared in EGM-2MV with 10 ng /ml of bFGF added as a source of endothelial cell stimulation. This assay may be used with a variety of endothelial cells with slight changes in growth medium and cell concentration. Dilutions of the protein batches to be tested are diluted as appropriate. Serum-free medium (GIBCO SFM) without bFGF is used as a non-stimulated control and Angiostatin or TSP-1 are included as a known inhibitory controls.

Briefly, LEC, BAECs or UTMECs are seeded in growth media at a density of 5000 to 2000 cells/well in a 96 well plate and placed at 37-C overnight. After the

overnight incubation of the cells, the growth media is removed and replaced with GIBCO EC-SFM. The cells are treated with the appropriate dilutions of the protein of interest or control protein sample(s) (prepared in SFM) in triplicate wells with additional bFGF to a concentration of 10 ng/ml. Once the cells have been treated with the samples, the plate(s) is/are placed back in the 37°C incubator for three days. After three days 10 ml of stock alamar blue (Biosource Cat# DAL1100) is added to each well and the plate(s) is/are placed back in the 37°C incubator for four hours. The plate(s) are then read at 530nm excitation and 590nm emission using the CytoFluor fluorescence reader. Direct output is recorded in relative fluorescence units.

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Alamar blue is an oxidation-reduction indicator that both fluoresces and changes color in response to chemical reduction of growth medium resulting from cell growth. As cells grow in culture, innate metabolic activity results in a chemical reduction of the immediate surrounding environment. Reduction related to growth causes the indicator to change from oxidized (non-fluorescent blue) form to reduced (fluorescent red) form. i.e. stimulated proliferation will produce a stronger signal and inhibited proliferation will produce a weaker signal and the total signal is proportional to the total number of cells as well as their metabolic activity. The background level of activity is observed with the starvation medium alone. This is compared to the output observed from the positive control samples (bFGF in growth medium) and protein dilutions.

Example 47: Detection of Inhibition of a Mixed Lymphocyte Reaction

This assay can be used to detect and evaluate inhibition of a Mixed

Lymphocyte Reaction (MLR) by gene products (e.g., isolated polypeptides).

Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by these polypeptides

since the peripheral blood mononuclear fraction used in this assay includes T, B and natural killer lymphocytes, as well as monocytes and dendritic cells.

Polypeptides of interest found to inhibit the MLR may find application in diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

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Briefly, PBMCs from human donors are purified by density gradient centrifugation using Lymphocyte Separation Medium (LSM®, density 1.0770 g/ml, Organon Teknika Corporation, West Chester, PA). PBMCs from two donors are adjusted to 2 x 10⁶ cells/ml in RPMI-1640 (Life Technologies, Grand Island, NY) supplemented with 10% FCS and 2 mM glutamine. PBMCs from a third donor is adjusted to 2 x 10⁵ cells/ml. Fifty microliters of PBMCs from each donor is added to wells of a 96-well round bottom microtiter plate. Dilutions of test materials (50 μl) is added in triplicate to microtiter wells. Test samples (of the protein of interest) are added for final dilution of 1:4; rhulL-2 (R&D Systems, Minneapolis, MN, catalog number 202-IL) is added to a final concentration of 1 μg/ml; anti-CD4 mAb (R&D Systems, clone 34930.11, catalog number MAB379) is added to a final concentration of 10 μg/ml. Cells are cultured for 7-8 days at 37°C in 5% CO₂, and 1 μC of [³H] thymidine is added to wells for the last 16 hrs of culture. Cells are harvested and thymidine incorporation determined using a Packard TopCount. Data is expressed as the mean and standard deviation of triplicate determinations.

Samples of the protein of interest are screened in separate experiments and compared to the negative control treatment, anti-CD4 mAb, which inhibits proliferation of lymphocytes and the positive control treatment, IL-2 (either as recombinant material or supernatant), which enhances proliferation of lymphocytes.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or

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antagonists and fragments and variants thereof.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties. Moreover, the hard copy of and the corresponding computer readable form of the Sequence Listing of Serial No. 60/124,270 are also incorporated herein by reference in their entireties.

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Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism reference 121 line	red to in the description N/A
on page 121 line	
B. IDENTIFICATIONOF DEPOSIT	Further deposits are identified on an additional sheet
Name of depositary institution American Type Culture Colle	ction
Transcordepositary insulation Amorican Type Conditio Cone	
Address of depositary institution (including postal code and count	(r)
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Manassas, Virginia 20110-2209	
United States of America	·
·	
Date of deposit	Accession Number
20 May 1997	209059
C. ADDITIONAL INDICATIONS (leave blank if not applicable	e) This information is continued on an additional sheet
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ATCC Deposit No. 209059

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

Page 2 ATCC Deposit No. 209059

DENMARK

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SWEDEN

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NETHERLANDS

	542		
Applicant's or agent's file reference number	PA106PCT	International application !	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	A. The indications made below relate to the microorganism referred to in the description			
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ATCC Deposit No. 209060

CANADA

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FINLAND

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UNITED KINGDOM

544

Page 2 ATCC Deposit No. 209060

DENMARK

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NETHERLANDS

Applicant's or agent's file PATOCOCT International application I		545	
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	The indication	ons made below relate to the i	microorganism refer	red to in the description
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ATCC Deposit No. 209061

CANADA

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UNITED KINGDOM

547

Page 2 ATCC Deposit No. 209061

DENMARK

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NETHERLANDS

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Applicant's or agent's file PA106PCT International application UNASSIGNED	 		
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 121				
B. IDENTIFICATIONOFDEPOSIT Further deposits are identified on an additional sheet Name of depositary institution American Type Culture Collection Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America Date of deposit 20 May 1997 Accession Number 20 May 1997 C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) Europe Europe and in respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC). E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g. "Accession Number of Deposit") This sheet was received with the international application Authorized officer Authorized officer	A. The indications made below relate to the microorganism referr			
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ATCC Deposit No. 209062

CANADA

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UNITED KINGDOM

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Page 2 ATCC Deposit No. 209062

DENMARK

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NETHERLANDS

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PA106PCT	International application i	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

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A. The indications made below relate to the microorganism referre	ed to in the description N/A		
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B. IDENTIFICATIONOFDEPOSIT	Further deposits are identified on an additional sheet		
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Address of depositary institution (including postal code and country	ry)		
10801 University Boulevard			
Manassas, Virginia 20110-2209 United States of America			
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D. DESIGNATED STATES FOR WHICH INDICATION	NS ARE MADE (if the indications are not for all designated States)		
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ATCC Deposit N . 209063

CANADA

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UNITED KINGDOM

Page 2 ATCC Deposit No. 209063

DENMARK

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NETHERLANDS

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Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

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ATCC Deposit No. 209064

CANADA

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UNITED KINGDOM

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Page 2 ATCC Deposit No. 209064

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NETHERLANDS

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Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

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CANADA

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UNITED KINGDOM

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Page 2 ATCC Deposit No. 209065

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NETHERLANDS

Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

				
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ATCC Deposit No. 209066

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UNITED KINGDOM

Page 2 ATCC Deposit No. 209066

DENMARK

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SWEDEN

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NETHERLANDS

	Applicant's or agent's file reference number	PA106PCT	International application I	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	A. The indications made below relate to the microorganism referred to in the description			
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ATCC Deposit No. 209067

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

Page 2 ATCC Deposit No. 209067

DENMARK

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NETHERLANDS

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Applicant's or agent's file reference number	PA106PCT	International application?	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description			
on page	N/A .		
B. IDENTIFICATIONOF DEPOSIT	Further deposits are identified on an additional sheet		
Name of depositary institution American Type Culture Colle	ection		
Address of depositary institution (including postal code and coun 10801 University Boulevard	lry)		
Manassas, Virginia 20110-2209			
United States of America			
Date of deposit	Accession Number		
20 May 1997	209068		
C. ADDITIONAL INDICATIONS (leave blank if not applicable	le) This information is continued on an additional sheet		
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D. DESIGNATED STATES FOR WHICH INDICATION	NS ARE MADE (if the indications are not for all designated States)		
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or until the date on which application has been refused	or withdrawn or is deemed to be withdrawn, only by		
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Form PCT/RO/134 (July 1992)

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ATCC Deposit N . 209068

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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UNITED KINGDOM

Page 2 ATCC Deposit No. 209068

DENMARK

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SWEDEN

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NETHERLANDS

Applicant's or agent's file	PA106PCT	International application!	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referr on page	ed to in the description N/A .			
B. IDENTIFICATIONOFDEPOSIT	Further deposits are identified on an additional sheet			
Name of depositary institution American Type Culture College	ction			
Address of depositary institution (including postal code and count 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	ny)			
Date of deposit	Accession Number			
20 May 1997	209069			
C. ADDITIONAL INDICATIONS (leave blank if not applicable	e) This information is continued on an additional sheet			
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).				
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ATCC Deposit No. 209069

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

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UNITED KINGDOM

Page 2 ATCC Deposit No. 209069

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NETHERLANDS

Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description	
on page	N/A .
B. IDENTIFICATIONOFDEPOSIT	Further deposits are identified on an additional sheet
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country)	
10801 University Boulevard	
Manassas, Virginia 20110-2209 United States of America	,
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Date of deposit	Accession Number
12 January 1998	209579
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet	
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D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
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ATCC Deposit No. 209579

CANADA

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NORWAY

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UNITED KINGDOM

Page 2 ATCC Deposit No. 209579

DENMARK

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NETHERLANDS

Applicant's or agent's file		International application	
	PA106PCT		UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

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A.	The indications m	ade below relate to the	microorganism referr	ed to in the description	
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ATCC Dep sit No. 209578

CANADA

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FINLAND

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UNITED KINGDOM

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Page 2 ATCC Deposit No. 209578

DENMARK

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NETHERLANDS

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Applicant's or agent's file		International application	
reference number	PA106PCT		UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	Theindica	tions made below relate to the	microorganism refer	red to in the description	
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В.	IDENTIFI	ICATION OF DEPOSIT		Further deposits are identified on an additional sheet	
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Ur	nited State	s of America			
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Da	te of deposit			Accession Number	
		16 July 1998		203067	
C.	ADDITIO	NAL INDICATIONS (lea	ve blank if not applicab	(e) This information is continued on an additional sheet	
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				he person requesting the sample (Rule 28 (4) EPC).	
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Form PCT/RO/134 (July 1992)

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ATCC Deposit No. 203067

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

580

Page 2 ATCC Deposit No. 203067

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

	701		
Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	A. The indications made below relate to the microorganism referred to in the description				
	on page _	121	,line	N/A	
B.	IDENTIFI	ICATION OF DEPOSIT		Further deposits are identified on an additional sheet	
Na	me of depos	itary institution American Ty	ype Culture Collec	ction	
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Ad	dress of de	positary institution (including	postal code and count	ry)	
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C.	ADDITIO	ONAL INDICATIONS (leav	e blank if not applicable	This information is continued on an additional sheet	
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D.	DESIGNA	ATED STATES FOR WHI	ICH INDICATION	NS ARE MADE (if the indications are not for all designated States)	
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	•	those designations in whi	ich a European P	atent is sought a sample of the deposited	
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				or withdrawn or is deemed to be withdrawn, only by	
uie	issue oi s	ouch a sample to an expe	it nominated by ti	ne person requesting the sample (Rule 28 (4) EPC).	
E.	SEPARA	TE FURNISHING OF IND	OICATIONS (leave b	lank if not applicable)	
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ATCC Deposit No. 203068

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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FINLAND

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UNITED KINGDOM

Page 2 ATCC Deposit No. 203068

DENMARK

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NETHERLANDS

		704	
Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	Theindica	ations made below relate to the m	nicroorganism referr	red to in the description
•	on page	121	,line	N/A
В.	IDENTIF	TCATIONOFDEPOSIT		Further deposits are identified on an additional sheet
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C.	ADDITI	ONAL INDICATIONS (leave	e blank if not applicable	This information is continued on an additional sheet
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D.	DESIGN	ATED STATES FOR WHI	CH INDICATION	NS ARE MADE (if the indications are not for all designated States)
	rope respect to	those designations in whi	ich a Furopean P	Patent is sought a sample of the deposited
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the	until trie o	such a sample to an exper	rt nominated by t	the person requesting the sample (Rule 28 (4) EPC).
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E.	SEPAR/	ATE FURNISHING OF IND	DICATIONS (leave)	blank if not applicable)
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ATCC Deposit No. 203609

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

Page 2 ATCC Deposit No. 203609

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

Applicant's or agent's file reference number PA106PCT International application UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A.	The indications made below relate to the microo	rganism referre	
	on page 121	line	NA
В.	IDENTIFICATIONOFDEPOSIT		Further deposits are identified on an additional sheet
Na	ume of depositary institution American Type C	Julture Collec	tion
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Ad	dress of depositary institution (including postal	code and country	y)
10	801 University Boulevard		
	anassas, Virginia 20110-2209		
Ui	nited States of America		
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C.	ADDITIONAL INDICATIONS (leave blank	c if not applicable)	This information is continued on an additional sheet
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D.	DESIGNATED STATES FOR WHICH I	NDICATION	IS ARE MADE (if the indications are not for all designated States)
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mic	croorganism will be made available until	the publicatio	on of the mention of the grant of the European patent
or	until the date on which application has be	een refused o	or withdrawn or is deemed to be withdrawn, only by
the	issue of such a sample to an expert ποι	minated by the	ne person requesting the sample (Rule 28 (4) EPC).
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E.	SEPARATE FURNISHING OF INDICA	TIONS (leave bi	lank if not applicable)
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	(703) 305-3539	I	

Form PCT/RO/134 (July 1992)

588

ATCC Deposit No. 203610

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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UNITED KINGDOM

Page 2 ATCC Deposit No. 203610

DENMARK

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SWEDEN

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NETHERLANDS

	590		
Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

PCT/US00/05882

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page			
B. IDENTIFICATIONOF DEPOSIT	Further deposits are identified on an additional sheet		
Name of depositary institution American Type Culture Collect	ction		
Address of depositary institution (including postal code and country 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	ry)		
Date of deposit	Accession Number		
17 November 1998	203485		
C. ADDITIONAL INDICATIONS (leave blank if not applicable	This information is continued on an additional sheet		
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).			
E. SEPARATE FURNISHING OF INDICATIONS (leave b	olank if not applicable)		
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")			
For receiving Office use only	For International Bureau use only		
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Form PCT/RO/134 (July 1992)

ATCC Deposit No. 203485

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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UNITED KINGDOM

Page 2 ATCC Deposit No. 203485

DENMARK

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NETHERLANDS

Applicant's or agent's file reference number PA106PCT International application UNASSIGNED				
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	reference number	PATOBECT	<u> </u>	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page121, lineN/A			
B. IDENTIFICATIONOF DEPOSIT	Further deposits are identified on an additional sheet		
Name of depositary institution American Type Culture Coll	lection		
Address of depositary institution (including postal code and count 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	ntry)		
Date of deposit	Accession Number		
18 June 1999	PTA-252		
C. ADDITIONAL INDICATIONS (leave blank if not applica	ble) This information is continued on an additional sheet		
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).			
E. SEPARATE FURNISHING OF INDICATIONS (leav.	e blank if not anni irable)		
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")			
For receiving Office use only This sheet was received with the international application	For International Bureau use only This sheet was received by the International Bureau on:		
Authorized officer PCT/Internat 1Appl Processing Div. (703) 305-3839			

Form PCT/RO/134 (July 1992)

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ATCC Deposit No. PTA-252

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

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UNITED KINGDOM

Page 2 ATCC Deposit No. PTA-252

DENMARK

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NETHERLANDS

Applicant's or agent's file reference number	PA106PCT	International application'	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page121 lineN/A			
B. IDENTIFICATIONOFDEPOSIT	Further deposits are identified on an additional sheet		
Name of depositary institution American Type Culture Colle	ction		
Address of depositary institution (including postal code and count 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	(יכו		
Date of deposit	Accession Number		
18 June 1999	PTA-253		
C. ADDITIONAL INDICATIONS (leave blank if not applicable	This information is continued on an additional sheet		
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent			
or until the date on which application has been refused the issue of such a sample to an expert nominated by the	or withdrawn or is deemed to be withdrawn, only by		
E. SEPARATE FURNISHING OF INDICATIONS (leave b	lank if not applicable)		
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")			
For receiving Office use only	For International Bureau use only		
This sheet was received with the international application	This sheet was received by the International Bureau on:		
Jeryl McDawe'l			
Authorized officer! Appl Processing Div. (703) 305-3639	Authorized officer		

Form PCT/RO/134 (July 1992)

597

ATCC Deposit No. PTA-253

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

Page 2 ATCC Deposit No. PTA-253

DENMARK

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SWEDEN

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NETHERLANDS

	599	·	
Applicant's or agent's file reference number	PA106PCT	International application	UNASSIGNED

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description				
٥	n page	121	, line	N/A
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Date	ofdeposit			Accession Number
	• • • • • • • • • • • • • • • • • • • •	22 December 199	9	PTA-1081
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C. A	DDITIONAL	L INDICATIONS (le	ave blank if not applicabl	e) This information is continued on an additional sheet
			•	•
D. D	ESIGNATE	D STATES FOR WI	IICH INDICATION	S ARE MADE (if the indications are not for all designated States)
Euro	pe			
				atent is sought a sample of the deposited
				on of the mention of the grant of the European patent or withdrawn or is deemed to be withdrawn, only by
				ne person requesting the sample (Rule 28 (4) EPC).
		F F		
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)				lank if not applicable)
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")				
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Form PCT/RO/134 (July 1992)

600

ATCC Deposit No. PTA-1081

CANADA

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UNITED KINGDOM

601

Page 2 ATCC Deposit No. PTA-1081

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NETHERLANDS

What Is Claimed Is:

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- 1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
- (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X, having biological activity;
 - (g) a polynucleotide which is a variant of SEQ ID NO:X;
 - (h) a polynucleotide which is an allelic variant of SEQ ID NO:X;
- (i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
- (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide

PCT/US00/05882

sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

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3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

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4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

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5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

- 6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
- 7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
 - 8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
- 30 9. A recombinant host cell produced by the method of claim 8.

- 10. The recombinant host cell of claim 9 comprising vector sequences.
- 11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
 - (b) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone, having biological activity;
 - (c) a polypeptide domain of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
 - (d) a polypeptide epitope of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
- (e) a full length protein of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
 - (f) a variant of SEQ ID NO:Y;

- (g) an allelic variant of SEQ ID NO:Y; or
- (h) a species homologue of the SEQ ID NO:Y.
- 20 12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the Nterminus.
- 13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
 - 14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
- 30 15. A method of making an isolated polypeptide comprising:

- (a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
 - (b) recovering said polypeptide.
- 5 16. The polypeptide produced by claim 15.
 - A method for preventing, treating, or ameliorating a medical condition, 17. comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

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- 18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.
 - 19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and
 - (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.
- 25 20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
 - (a) contacting the polypeptide of claim 11 with a binding partner; and
 - (b) determining whether the binding partner effects an activity of the polypeptide.

- 21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
- 22. A method of identifying an activity in a biological assay, wherein the method comprises:
- 5 (a) expressing SEQ ID NO:X in a cell;
 - (b) isolating the supernatant;
 - (c) detecting an activity in a biological assay; and
 - (d) identifying the protein in the supernatant having the activity.
- 10 23. The product produced by the method of claim 20.

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<211> 1101

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<213> Homo sapiens

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<213> Homo sapiens
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<212> DNA

<213> Homo sapiens

<400> 11

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<213> Homo sapiens

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<222> (1102)
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<223> n equals a,t,g, or c

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<211> 559

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<222> (613)
<223> n equals a,t,g, or c
<220>
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<222> (616)
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<210> 18
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<213> Homo sapiens
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<223> n equals a,t,g, or c
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<222> (531)
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<223> n equals a,t,g, or c
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<222> (547)
<223> n equals a,t,g, or c
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<222> (556)
<223> n equals a,t,g, or c
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tccctgggta catcaaactg tactccacag ataacagaca ccagtgagtt tttcatggtt 480
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<222> (55)
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<222> (1355)
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<223> n equals a,t,g, or c
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<222> (1162)
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WO 00/55350 PCT/US00/05882

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<223> n equals a,t,g, or c

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taatgttggt gtggagtttt catgacagaa tatacacatt ttgtaaatct gtacttttt 900
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<221> misc feature
<222> (1988)
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egecteegee geetageget gtteeegggt gtggegetge ttettgeege ggeeegeete 180
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acacqtacqa cqaqtacaaa aaggqcttcc tggaccaggc atctgggagt gcagtqctqc 180
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<221> misc feature

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tccaaatgaa aaacataatt gcttcaaaac acttacacag ttggaaagtt atatgtaagt 420
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<222> (501)

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<222> (575)
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<400> 53
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tggaaactcg cagagtcctg gtgggtgagc agcagcagtg ccasgatgcc aagagccagc 180
agaaggagca gatgttgctg ctggagaaka agagtgctgc ttactcccag gtgcttctcc 240
gctgcctcac tttgctgcag aggcttcttc aagaacaccg gctgaagact caatccgagc 300
tagaccgcat caatgcccag tacctggaag tcaagtgcgg tgctatgatc cttaagctga 360
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gtctgattag ggaccgtttg gagggagcca ttcacctaca ggagcaggac atggagaact 480
caagacaggt cctgaactcc tatgaggtcc ttggggagga gtttgacagg ctggtgaaag 540
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aggtetaccg ttgagentcg neagggeeag gagacatgge ttetgeatag etgetgeete 660
ctaatcttcc tgctagtggg accaccttca cctggggctg ccttcagtac aagggagtgt 720
ggaanatstt acgettgaaa cactgeagte atttaggeae teteetggtt tetetttatt 780
ttttatgact gggcctcttc tggaaaatct agcaaggaga tttatataat ttttatgcat 840
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attawaaaaa aaaaaaaaa
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<210> 54
<211> 1090
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
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<223> n equals a,t,g, or c
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43

<400> 54

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tgtctttata gatttcttta aatttcctta tagaaccatt aatagaaaat cattacattt 480
aaaatatacc ttacagcaaa agcatccaaa taagtatagg gtttatgtcc ttatttttct 540
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tttatttcag tgggcacttt tccattttac cactgtacca ttatttggtt cctggagtta 660
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                                                                  1090
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<210> 55
<211> 1464
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (766)
<223> n equals a,t,g, or c
<400> 55
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tectgtgeaa geteagettg gagggtgate aetetacace eccaagtgea tatgggtetg 180
tcaaagccta tactaacttt gatgctgagc gggatgcttt gaacattgaa acagccatca 240
agaccaaagg tgtggatgag gtcaccattg tcaacatttt gaccaaccgc agcaatgcac 300
agagacagga tattgccttc gcctaccaga gaaggaccaa aaaggaactt gcatcagcac 360
tgaagtcagc cttatctggc cacctggaga cggtgatttt gggcctattg aagacacctg 420
ctcagtatga cgcttctgag ctaaaagctt ccatgaaggg gctgggaacc gacgaggact 480
ctctcattga gatcatctgc tccagaacca accaggagct gcaggaaatt aacagagtct 540
acaaggaaat gtacaagact gatctggaga aggacattat ttcggacaca tctggtgact 600
tecgeaaget gatggttgee etggeaaagg gtagaagage agaggatgge tetgteattg 660
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```

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ttccaaggag ttggaagtga agtctatgat gtgaaacact ttgcctcctg tgtactgtgt 1380
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ggggcccgka cccattggcc ttag
<210> 56
<211> 985
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (875)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (962)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (973)
<223> n equals a,t,g, or c
<400> 56
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gactggagga tettgtacce agagattece egtaagetee gagagetgga ageegaggge 180
tacaagctgg tgatcttcac caaccagatg agcatcgggc gcggggaagct gccagccgag 240
gagttcaagg ccaaggtgga ggctgtggtg gagaagctgg gggtcccctt ccaggtgctg 300
gtggccacgc acgcaggett gtaccggaag ccggtgacgg gcatgtggga ccatctgcag 360
gagcaggcca acgacggcac gcccatatcc atcggggaca gcatctttgt gggagacgca 420
geeggaegee eggeeaactg ggeeeegggg eggaagaaga aagaettete etgegeegat 480
egectgtttg eceteaacet tggeetgeee ttegecaege etgaggagtt ettteteaag 540
tggccagcag ccggcttcga gctcccagcc tttgatccga ggactgtctc ccgctcaggg 600
cctctctgcc tccccgagtc cagggccctc ctgagcgcca cccggangtg gttgtcgcag 660
tgggattccc tggggccggg aagtccacct ttctcaagaa gcacctcgtg tcggccggat 720
atgtccacgt gaacagggac acgctaggct cctggcagcg ctgtgtgacc acgtgtgara 780
cagocotgaa gcaagggaaa cgggtcgcca tcgacaacac aaacccagac gccgcgagcc 840
gcgccaggta cgtccartgt gcccgagccg cgggngtacc cctgccgctg cttcctcttc 900
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<211> 1246
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gccattggaa ggggcatatg tgtgttgctg ggtatttccc tggaggatac gcagaaggaa 180
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<210> 58
<211> 1966
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1926)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1942)
<223> n equals a,t,g, or c
<400> 58
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tgaaccttca caatttgtta aaatccaaga acctttgttt aaacaaatcg ccaagtgtgt 180
atctagcccc cattttcagg tggcagaaag agcactctat tattggaata atgaatacat 240
catgagtttg atagargaaa actctaacgt catccttccc atcatgtttt ccagccttta 300
taggatttca aaagaacatt ggaatccggc tattgtggcg ttggtgtaca atgtgttgaa 360
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caaaggtgca tcgtgaccaa attgtttaaa aaaaaaaaac aaaaaaaaca aaatctaggg 1860
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                                                                 1966
<210> 59
<211> 1611
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (7)
<223> n equals a,t,g, or c
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tototggtog titagotgaa atgootgoag atagtggata tocagootat ottggtgooc 300
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<210> 60
<211>. 1849
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<220>
<221> misc feature
<222> (977)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (1846)
<223> n equals a,t,g, or c
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<211> 233
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<213> Homo sapiens
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<210> 62
<211> 2333
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (6)
<223> n equals a,t,g, or c
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<222> (7)
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<221> misc feature
<222> (14)
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<222> (2331)
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2333
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<210> 63
<211> 1470
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1410)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1414)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1419)
<223> n equals a,t,g, or c
<400> 63
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                                                                  1470
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<210> 64
<211> 939
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<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (3)
<223> n equals a,t,g, or c
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<222> (4)
<223> n equals a,t,g, or c
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<222> (11)
<223> n equals a,t,g, or c
<400> 64
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<210> 65
<211> 2068
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (308)
<223> n equals a,t,g, or c
<400> 65
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acaagecetg aacgageace teageaegeg tagtatgtee aggggtaete actgteecag 180
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<223> n equals a,t,g, or c

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 ccctgcangc tyccaagcar gcaaaggccg gcgtgtgcag ccccagtggt cccctcctgc 360
 tgggacccas catgcagact ccacctttac aacagcctca ccaggaacaa ggaagtgttc 420
 atacctcaag atgggaaaaa ggtgacgtgg tattgctgtg ggccaaccgt ctatgacgca 480
 teteacatgg ggcacgecag gteetacate tettttgata tettgagaag agtgttgaag 540
 gattacttca aatttgatgt cttttattgc atgaacatta cggatattga tgacaagatc 600
 atcaagaggg cccggcagaa ccacctgttc gagcagtatc gggagaagag gcctgaagcg 660
 gcacagetet tggaggatgt teaggeegee etgaageeat ttteagtaaa attaaatgag 720
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<210> 66
<211> 1391
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)
<223>.n equals a,t,g, or c
<220>
<221> misc feature
<222> (16)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (20)
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<212> DNA

<213> Homo sapiens

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<221> misc feature
<222> (25)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (27)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1343)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1358)
<223> n equals a,t,g, or c
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gttagcctaa gtcacttcca ccctccaatg ttgtgaatgc agtctctagc attcgctatt 180
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gacceggaat eggatectag teccaecece teegeteeag getteettet geaacaggeg 480
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<210> 67
<211> 659
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<221> misc feature
<222> (139)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (475)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (585)
<223> n equals a,t,g, or c
<400> 67
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<210> 68
<211> 2981
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (2858)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (2948)
<223> n equals a,t,g, or c
<400> 68
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tatgetttea tteteeteet gageactgte gtateetata teatgeagag aaaagagatg 300
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                                                                  2981
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<210> 69

<211> 603

<212> DNA

<213> Homo sapiens

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<222> (584)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (590)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (595)
<223> n equals a,t,g, or c
<400> 69
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                                                                   603
<210> 70
<211> 1101
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (195)
<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (1080)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (1081)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1090)
<223> n equals a,t,g, or c
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<400> 70
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71

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72

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<211> 1037

<212> DNA

<213> Homo sapiens

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<213> Homo sapiens

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<222> (1571)
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PCT/US00/05882

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101

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PCT/US00/05882

102

WO 00/55350

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PCT/US00/05882 WO 00/55350

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106

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ccqqccqqcq gaccqaaqaa cqcaqqaaqq qqqccqqqqq gacccqcccc cqqccqqccq 180
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PCT/US00/05882 WO 00/55350

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atgaagcagt gttttatcat gtgtatttca gcaggtcttc ttgaaattta actaaaaata 540
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<213> Homo sapiens

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<222> (119)

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<211> 817

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<213> Homo sapiens

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139

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cgcaagttag atcgatttca tcccaaagaa cttctggagt gtgcatttga tattgtcact 360
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<211> 1987
<212> DNA
<213> Homo sapiens
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<220>

<221> misc feature

<222> (523)

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gagttaataa aaatttotga gggaacagga ttoagaatao acatgatooa caaagcagca 840
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<211> 1737
<212> DNA
<213> Homo sapiens
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cacataaagc catgctgttt ttggtcaaac tgtgtaaact ggaaaaattc acatcatttc 240
tttttctttc tcaaatctgt gatctctttt ctttatcctg tttctttgtt cctttcgttt 360
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1132)
<223> n equals a,t,g, or c
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<213> Homo sapiens
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<211> 3787
<212> DNA
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<222> (155)
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PCT/US00/05882

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1512
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<222> (384)
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PCT/US00/05882

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<211> 1129
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (807)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<222> (678)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (897)
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<222> (898)
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PCT/US00/05882

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205

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<221> misc feature
<222> (1496)
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<222> (1523)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<222> (1501)
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<222> (1506)
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (632)
<223> n equals a,t,g, or c
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<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (558)
<223> n equals a,t,g, or c
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PCT/US00/05882

WO 00/55350

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<211> 570
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (567)
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<222> (1038)
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<211> 1394
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<213> Homo sapiens
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249

<210> 298

<211> 1666

<212> DNA

<213> Homo sapiens

<400> 298

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<213> Homo sapiens
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<222> (4)
<223> n equals a,t,g, or c
<220>
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<222> (402)
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<210> 334
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<212> DNA
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<222> (59)
<223> n equals a,t,g, or c
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<220>

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 <223> n equals a,t,g, or c
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<221> misc feature
<222> (1006)
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<222> (1023)
<223> n equals a,t,g, or c
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testiftings atcaptions agraectifty stacages at gleactesty gegacestyg 300
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<211> 2127
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (72)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (2098)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (2114)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (2117)
<223> n equals a,t,g, or c
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<212> DNA
<213> Homo sapiens
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<222> (.334)
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<222> (829)
<223> n equals a,t,g, or c
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<222> (847)
<223> n equals a,t,g, or c
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tecceactee titecteacy ecaagetety actitecyty etecacyate ecgeggetee 180
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cttcttccag agagatctct tggcagagtg agggcctgga gataaccagc tttggattat 720
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<211> 702
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<223> n equals a,t,g, or c
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<400> 338

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<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (679)
<223> n equals a,t,g, or c
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aacccgcaaa gagtaagacg gcagcggcan cctctgaaaa gaatcggggc ccaagaaaag 180
geggtegtgt tategeteec argaaggege gegtegtgea geageaaaag eteaagaaga 240
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ccctacctcc atatgggacc ttgcaagtca tcccacaggc tgcactgtca ggaagaggac 480
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<211> 875
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (791)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (813)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (830)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (861)
<223> n equals a,t,g, or c
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cacacacaaa gataacagta cctagagaga gagtgtgtgt gagtgtgcgt gtctctgtgt 180
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<211> 1448
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<213> Homo sapiens
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<221> misc feature
<222> (1427)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1432)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1440)
<223> n equals a,t,g, or c
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tetgttttee atcecettea ggteetteet egggaggegg egaaggeggt ceaecetgeg 180
egtgateett yatgeeegge eeetgeeeet eeeteegggt ggaactteee eeteaeegee 240
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<211> 843
<212> DNA
<213> Homo sapiens
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<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<222> (841)
<223> n equals a,t,g, or c
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ccgctggcac tggagcagtg ggtccctggt ctcctacaag tcctggggca ttggagcccc 480
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<213> Homo sapiens
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<211> 1273
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (6)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (483)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (1247)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1262)
<223> n equals a,t,g, or c
<400> 342
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<210> 343
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<212> DNA
<213> Homo sapiens
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<222> (1251)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1267)
<223> n equals a,t,g, or c
<400> 343
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PCT/US00/05882

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294

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302

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303

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<210> 377
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<223> n equals a,t,g, or c
<400> 377
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<213> Homo sapiens
<220>
<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (2565)
<223> n equals a,t,g, or c
<400> 378
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<211> 1680
<212> DNA
<213> Homo sapiens
<400> 379
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<211> 1267
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (4)
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<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (214)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1165)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1255)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1262)
<223> n equals a,t,g, or c
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atcatttctt tagagggaag gaataatcat tcaaatgaac tttaaaaaaag caaatttcat 660
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<210> 381
<211> 1031
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (1015)
<223> n equals a,t,g, or c
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<211> 1597
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1577)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1579)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1597)
<223> n equals a,t,g, or c
<400> 382
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ageggetgte caategagte gtgegtgtgt tgggetgtaa eeegggteee atgaeeetee 180
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<210> 383
<211> 175
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (95)
<223> n equals a,t,g, or c
<400> 383
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<210> 384
<211> 2171
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (2166)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (2170)
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<223> n equals a,t,g, or c
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<210> 385

<211> 2364

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (19)

<223> n equals a,t,g, or c

<400> 385

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324

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328

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331

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PCT/US00/05882

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<221> misc feature
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<221> misc feature
<222> (107)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (440)
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<210> 407
<211> 1693
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1548)
<223> n equals a,t,g, or c
<400> 407
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1693
tcgagacagt tct
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<210> 408 <211> 1342

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<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (107)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1332)
<223> n equals a,t,g, or c
<400> 408
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<211> 2417
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (107)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (680)
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<223> n equals a,t,g, or c

<400> 409

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aggaagegge tetgetgagg tteaagggge ceeageacag tgtggcatce gtteagettt 180
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<210> 410

<211> 1401

<212> DNA

<213> Homo sapiens

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<221> misc feature
<222> (1394)
<223> n equals a,t,g, or c
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tgatcccaaa atgcaaactg acaaaccttt tgaccagacc acaattagtc tgcagatggg 180
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<210> 411
<211> 3016
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (399)
<223> n equals a,t,g, or c
<400> 411
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ccggggctgg tgattggagg aaaccccgtg tctgcggacg gctgtagcct gtgagcagcg 120
agatecaggg acagagtete agectegeeg etgetgeege egeegeegee eagagactge 180
tgagcccgtc cgtccgccgc caccacccac tccggacaca gaacatccag tcatggataa 240
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agagaaaatt gagacggagc taagagatat ctgcaatgat gtactgtctc ttttggaaaa 540
gttcttgatc cccaatgctt cacaagcaga gagcaaagtc ttctatttga aaatgaaagg 600
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345

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<210> 412

<211> 958

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (930)

<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (934)
<223> n equals a,t,g, or c
<400> 412
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<210> 413
<211> 500
<212> DNA
<213> Homo sapiens
<400> 413
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                                                              500
<210> 414
<211> 3397
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
<222> (15)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (24)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (3081)
<223> n equals a,t,q, or c
<400> 414
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<222> (1611)

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<211> 1616
<212> DNA
<213> Homo sapiens
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<222> (12)
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<221> misc feature
<222> (1610)
<223> n equals a,t,g, or c
<220>
<221> misc. feature
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<221> misc feature
<222> (1616)
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<211> 1815
<212> DNA
<213> Homo sapiens
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<222> (270)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1184)
<223> n equals a,t,g, or c
<400> 417
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352

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<221> misc feature
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<221> misc feature

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<223> n equals a,t,g, or c
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375

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<213> Homo sapiens
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<223> n equals a,t,g, or c
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380

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<222> (865)
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382

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<213> Homo sapiens

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<212> DNA

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389

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<213> Homo sapiens

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gaggaatggg atttaatgac ctttgatgcc aacccatatg acagcgtgaa aaaaatcaaa 180
gaacatgtcc ggtctaagac caaggttcct gtgcaggacc aggttctttt gctgggctcc 240
aagatettaa ageeacqqag aageetetea tettatggca ttgacaaaga gaagaccate 300
caccttaccc tgaaagtggt gaagcccagt gatgaggagc tgcccttgtt tcttgtggag 360
teaggtgatg aggeaaagag geaceteete eaggtgegaa ggteeagete agtggeacaa 420
gtgaaagcaa tgatcgagac taagacgggt ataatccctg agacccagat tgtgacttgc 480
aatggaaaga gactggaaga tgggaagatg atggcagatt acggcatcag aaagggcaac 540
ttactcttcc tggcatstta ttgtattgga gggtgaccac cctgggcatg gggtgttggc 600
aggggtcaaa aagcttattt cttttaatct cttactcaac gaacacatct tctgatgatt 660
tcccaaaatt aatgagaatg agatgagtag agtaagattt gggtgggatg ggtaggatga 720
agtatattgc ccaactctat gtttctttga ttctaacaca attaattaag tgacatgatt 780
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<210> 476
<211> 1141
<212> DNA
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<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c
<400> 476
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tgacagcgtt taacaaagct tagagaaacc tccaggagac tgctatcatg gcagagaagc 180
ccaagctcca ctacttcaat gcacggggca gaatggagtc cacccggtgg ctcctggctg 240
caqctqqaqt aqaqtttqaa qagaaattta taaaatctgc agaagatttg gacaagttaa 300
gaaatgatgg atatttgatg ttccagcaag tgccaatggt tgagattgat gggatgaagc 360
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1141
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<211> 1102
<212> DNA
<213> Homo sapiens
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tectecaget geoceagtga gggeecacee tgeetgeace teegeggget gaetggeeac 960
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aaaaaaacc ccgggggggg gc
<210> 478
<211> 4201
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (4077)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (4161)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (4186)
<223> n equals a,t,g, or c
<400> 478
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cetecegety etgetgeege tycegeety agteactgee tycegeagete eggeegeety 120
gctccccata ctagtcgccg atatttggag ttcttacaac atggcagaca ttgacaacaa 180
agaacagtct gaacttgatc aagatttgga tgatgttgaa gaagtagaag aagaggaaac 240
tggtgaagaa acaaaactca aagcacgtca gctaactgtt cagatgatgc aaaatcctca 300
gattettgea gecetteaag aaagaettga tggtetggta gaaacaccaa caggatacat 360
tgaaagcctg cctagggtag ttaaaagacg agtgaatgct ctcaaaaacc tgcaagttaa 420
atgtgcacag atagaagcca aattctatga ggaagttcay gatcttgaaa ggaagtatgc 480
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tacggaagaa gaatgtgaat ggaaaccaga tgaagaagat gagatttcgg aggaattgaa 600
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gatgcatttt gaactttaat ataggaaggg gaagaagaag gagatgagga aaatgatcca 1560
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<210> 479

<211> 787

<212> DNA

<213> Homo sapiens

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<221> misc feature
<222> (780)
<223> n equals a,t,g, or c
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tggaggttgt agtaccgccc ccagagccaa ttttccactt ccgcktccgg cgctgcggca 180
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787
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<210> 480
<211> 731
<212> DNA
<213> Homo sapiens
<400> 480
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731
aaaaaaaaa a
<210> 481
<211> 1119
<212> DNA
<213> Homo sapiens
<400> 481
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ccccagtccc ccccacccgc gcgtggcggc gccggctccc tagccaccgs ggccccaccc 180
tottccggcc tcagctgtcc gggctgcttt cgcctccgcc tgtggatgct gcgcctctcc 240
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<210> 482
<211> 2056
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (137)
<223> n equals a,t,g, or c
<400> 482
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<211> 887
<212> DNA
<213> Homo sapiens
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887
<210> 484
<211> 1878
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1446)
<223> n equals a,t,g, or c
<400> 484
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409

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423

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<222> (36)

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<221> misc feature
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<223> n equals a,t,g, or c
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<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (457)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (492)
<223> n equals a,t,g, or c
<400> 503
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gtggcaagca ccaaccccat aaagtgacac agtacaagaa gggcaaggat tctctgtacg 180
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<222> (1974)
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<222> (1976)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (2002)
<223> n equals a,t,g, or c
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PCT/US00/05882

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<212> DNA
<213> Homo sapiens
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<222> (30)
<223> n equals a,t,g, or c
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aacttctgag cctcagtttt ctcctttgca aattaataat tacatacctt tatagatttt 360
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<221> misc feature
<222> (1064)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (1106)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<211> 2048

<212> DNA

<213> Homo sapiens

<400> 514

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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

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441

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<211> 1169
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<210> 523
<211> 799
<212> DNA
<213> Homo sapiens
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (758)
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gataaaacct aagttgcaat teeggtttte eteaagatet aagacatgtt acaaatggtt 240
aattgeettt gttteteget ttggtaacat etteeegeet eaggtattte eegeettgaa 300
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<213> Homo sapiens
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<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (36)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (40)
<223> n equals a,t,g, or c
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yacagatggg accatgaact coggacacag cttcagecag accecttcgg cctccttcca 180
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gcagaatete aacgacegee tggeeteeta eetggagaag gttegegeee tggaggagge 420
caacatgaag ctggaaagcc gcatcctgaa atggcaccag cagagagatc ctggcagtaa 480
gaaagattat teecagtatg aggaaaacat cacacacetg caggagcaga tagtggatgg 540
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<220>
<221> misc feature
<222> (526)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (557)
<223> n equals a,t,g, or c
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<210> 526
<211> 2023
<212> DNA
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<213> Homo sapiens
<220>
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<222> (12)
<223> n equals a,t,g, or c
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<211> 2847
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (286)
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<221> misc feature
<222> (290)
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<220>
<221> misc feature
<222> (2842)
<223> n equals a,t,g, or c
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<212> DNA

<213> Homo sapiens

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<211> 816
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (8)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (22)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (94)
<223> n equals a,t,g, or c
<400> 528
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aaggtacagg cctcagggtc cctgctgtag acggggcggg ggagagtacg atgggtgggg 120
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<223> n equals a,t,g, or c
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caargacete caagacaggt gaggettaga teecategea gagaageeet ggggtgarga 420
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kggatgcctg ggaatgctac tnggggaaan cagcatccaa canct
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<213> Homo sapiens
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<223> n equals a,t,g, or c

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gaaatgattc tggggaccat tctgaccaca tgcattacta tcagggtaaa aaatatttcc 660
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<211> 1800
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<213> Homo sapiens
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WO 00/55350

458

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PCT/US00/05882

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463

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<222> (1287)
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aattggagtc tgtttgctgt taatttcttt gtgggggcag caggagcctc tcagcttttt 540
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<211> 1052
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<222> (937)
<223> n equals a,t,g, or c
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<222> (943)
<223> n equals a,t,g, or c
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<222> (1004)
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<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (1051)
<223> n equals a,t,g, or c
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<211> 2093
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<213> Homo sapiens
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<221> misc feature
<222> (969)
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<222> (1422)
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<222> (1481)
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<211> 562

<212> DNA

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WO 00/55350

<222> (444)

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<223> n equals a,t,g, or c
<220>
<221> misc feature
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<221> misc feature
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<221> misc feature
<222> (507)
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<222> (160)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (174)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (341)
<223> n equals a,t,g, or c
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<220>

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<221> misc feature
<222> (389)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (413)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (444)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (450)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (468)
<223> n equals a,t,g, or c
<400> 601
gcctacacgc cgccgcttgt gctgcagcca tgtctctagt gatccctgaa aagttccagc 60
atattttgcg agtactcaac accaacatcg atgggcggcg gaaaatagcc tttgccatca 120
ctgccattaa gggtgtgggc cgaanatatg ctcatgtggn gttgaggaaa gnanacattg 180
acctnaccaa nagggcggna gaactcactg angatgangt ggaacgtgtg atcaccatta 240
tgcagaaten acgccagtac aagateccag actggttett gaacagacag aatgatngta 300
angatnaatc tacttcaagc taacatgcta tcatttctac nttgagtact gctaaggttt 360
ctttccacaa cttgtacaca atgttattna ctgcccagtt tataatttcc ctnttggttc 420
ccattttaag acttatttaa ttantatgen ttttaaattt ttgagaentg ataga
<210> 602
<211> 288
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (84)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (100)
<223> n equals a,t,g, or c
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<400> 602
cacattetea ggaactetee ttetttgggg ageeteagat gggaagggae tegageecea 60
cctgtccctg gactctggaa tgtntggctg aagttgaggn tctcttactc tctaggccac 120
ggaattaacc cgagcaggca tggaggcctc tgctctcacc tcatcagcag tgaccagtgt 180
ggccaaagtg gtcagggtgg cctctggctc tgccgtagtt ttgcccctgg ccaggattgc 240
tacagttgtg attggaggag ttgtggccat ggcggctgtg cccatggt
<210> 603
<211> 432
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (365)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (408)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (416)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (421)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (425)
<223> n equals a,t,g, or c
<400> 603
ggegeeeegg agagetettg egegtettgt tettgeetgg tgteggtggt tagtttetge 60
gacttgtgtt gggactgctg ataggaagat gtcttcagga aatgctaaaa ttgggcaccc 120
tgcccccaac ttcaaagcca cagctgttat gccagatggt cagtttaaag atatcagcct 180
gtctgactac aaaaggaaaa tatgttgtgt tcttctttta ccctcttgac ttcacctttg 240
tgtgccccac ggagatcatt gctttcagtg atagggcaga agaatttaag aaactcaact 300
gccaagtgat tggtgcttct gtggattctc acttctgtca tctagcatgg gtcaatacac 360
ctaanaaaca aggaggactg ggacccatga acattccttt ggtatcanac ccaacncaca 420
                                                                   432
nttgntcagg at
<210> 604
<211> 371
<212> DNA
<213> Homo sapiens
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<220>
<221> misc feature
<222> (282)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (291)
<223> n equals a,t,g, or c
<400> 604
atttagtgtg ataaggagaa gaacctgctg catgtcacag acaccggtgt aggaatgacc 60
agagaagagt tggttaaaaa ccttggtacc atagccaaat ctgggacaag cgagtttta 120
aacaaaatga ctgaagcaca ggaagatggc cagtcaactt ctgatttgat tggccagttt 180
ggtgtcggtt tctattccgc cttccttgta gcagataagg ttattgtcac ttcaaaacac 240
aacaacgata cccagcacat ctgggagtct gactccaatg anttttctgt naattgctga 300
cccaagaggg aaacactcta ggacggggga acgacaattt acgtggagta tggaccaatt 360
tccttattaa g
<210> 605
<211> 392
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (292)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (322)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (330)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (331)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (342)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
<222> (363)
<223> n equals a,t,g, or c
<400> 605
ggcacagccg gcatcgtggt gtgttcttga ctccgctgct cgccatgtct tctcacaaga 60
ctttcaggat taagcgattc ctggccaaga aacaaaagca aaatcgtccc attccccagt 120
ggattcggat gaaaactggg aaataaaatc aggtacaact ccaaaaggag acattggaga 180
agaaccaagc tgggtctatg aaggaattgc acatgagatg gcacacatat ttatgctgtc 240
tggaaggtgc acgatccatg ttaccatatg caagctggaa aatgtgcacc antatctggg 300
agattttcga cgtgtttttc cnctctggan nctgtttatg gnacaaggtt ggtttggttt 360
ggntccatta aattaaatta ggtaaaggcc cc
                                                                   392
<210> 606
<211> 442
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (255)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (312)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (368)
<223> n equals a,t,g, or c
<400> 606
gcgtcttcag ggtggaagcc tggcgcacgt ccggagagac acccgccatt tcacccagta 60
agegggeeeg geetgeggag gtgggeggea tgeageteeg etttgeeegg eteteegage 120
acgccacggc ccccacccgg ggctccgcgc gcgccgcggg ctacgacctg tacagtgcct 180
atgattacac aataccacct atggagaaag ctgttgtgaa aacggacatt cagatagcgc 240
tcccttctgg gtgtnatgga agagtggctc cacggtcagg cttggctgca aaacacttta 300
ttgatgtagg antggtgtca tagatgaaga ttataagagg aatgttggtg ttgtactgtt 360
taatttingg caagaaagtt tgaagtcaaa aaaggtgatc gaattgcaca gtcattigca 420
acggattttt tatccagaaa ta
                                                                   442
<210> 607
<211> 182
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (53)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (124)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (132)
<223> n equals a,t,g, or c
<400> 607
gcaccatggc ggttggcaag aacaagcgcc ttacgaaagg cggcaaaaag ggngccaaga 60
agaaagtggt tgatccattt tttaagaaag attggtatga tgtgaaagca cctgctatgt 120
tcantataag anatattgga aagacgctcg tcaccaggac ccaaggaacc aaaattgcat 180
<210> 608
<211> 673
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (561)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (569)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (603)
<223> n equals a,t,g, or c
<221> misc feature
<222> (604)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (627)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (630)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (652)
<223> n equals a,t,g, or c
<400> 608
nncaaaatta accectaat aaaattaatt aaccactcac tcatcgacct ccccaccca 60
tccaacatct ccgcatgatg aaacttcggc tcactccttg gcgcctgcct gatcctccaa 120
atcaccacag gactattcct agccatgcac tactcaccag acgcctcaac cgccttttca 180
tcaatcgccc acatcactcg agacgtaaat tatggctgaa tcatccgctg ccttcacgcc 240
aatggcgcct caatattctt tatctgcctc ttcctacaca tcgggcgagg cctatattac 300
ggatcatttc tctactcaga aacctgaaac atcggcatta tcctcctgct tgcaactata 360
gcaacagcct tcataggcta tgtcctcccg tgaggccaaa tatcattctg aggggccaca 420
gtaattacaa acttactatc cgccatccca tacattggga cagacctagt tcaatgaatc 480
tgaggaggct actcagtaga cagtcccacc ctcacacgat tctttacctt tcacttcatc 540
ttgcccttca ttattggcag ncctacagna ctcacctcta ttttttgccg aaacggggat 600
canneaacce cettagggaa teacetneen ttteegataa aaateaacct tneaccettt 660
actacacaat cat
<210> 609
<211> 553
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (377)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (449)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (497)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (536)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (545)
<223> n equals a,t,g, or c
<400> 609
gcggacgcgt gggttttaat acaaatgtta tttatagttt acaatgaatg cactgcataa 60
aaacttttgg acgacaatgg gaacattgct gaagaactga gcattctcaa atggaacaca 120
gacagtgtag aagaattcct gagtgaaaag ttggaacgca tataaatctt gcttaaattt 180
tgtcctatcc ttttgttacc ttatcaaatg aaatattaca gcacctagaa aataatttag 240
ttttgcttgc ttccattgat cagtctttta cttgaggcat taaatatcta attaaatcgt 300
gaaatggcag tatagtccat gatatctaag gagttggcaa gcttaacaaa acccattttt 360
tataaatgtc catccinctg cattigtiga taccactaac aaaatgcitt gtaacagact 420
tgcggttaat tatgcaaatg atagtttgng ataattgggg ccaagtttta cgaacaacag 480
atttctaaat tagaganggt taccaggaca gatgatacta tgcctaaggg ctgggngccc 540
                                                                   553
ttttnaagga aga
<210> 610
<211> 458
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (17)
<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (18)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (215)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (225)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (281)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (312)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (314)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (316)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (344)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (369)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (412)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (430)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (442)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (456)
<223> n equals a,t,g, or c
<400> 610
acccacgcgt ccggctnncc gatgagacca atatatgcaa tggtaagcca gtagatggac 60
tgactacttt gcgcaatggg acattagttg cattccgagg tcattatttc tggatgctaa 120
gtccattcag tccaccatct ccagctcgca gaattactga agttttgggg aatcctttcc 180
cccattgata ctgttttact aaggggaatt tttcnagaaa aggtngcagc attcagcagt 240
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atatttataa acaggaacct gtacagaagt gcccttggaa naaggcctgc tctaaaatta 300
tccagtggta tngngnaacg acacaggtta agagacgtcg cttnaacgtg ctaaaaggac 360
ctttccaana cacaccatca gaatccataa tcacctgcca aatggggtat cnagaccaag 420
gggcctccan aaggagttaa gnggttaccg tggggngg
<210> 611
<211> 565
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (5)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (469)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (471)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (534)
<223> n equals a,t,g, or c
<400> 611
aagenganae caaceeteae taaagggaae aaaagetgga getecaeege ggtgeggeeg 60
ctctagaact agtggatccc ccgggctgca ggaattcggc acgaggttgc agtgagccga 120
gatogoacca ttgcactoca gtotgggcaa cagagtgaga ttccgtotca aaaaaaaaaa 180
gaaaaggaaa aaaaaatagc attatacctc ttccttgtct caaccgccat gaaaattctg 240
aacactccaa attcagttga ataatccaaa acaaaattta taagtataaa ataattttac 300
ttcttatagt aatagtatac tttaaaaagc ctcagggtat attatcttct aaacagctac 360
aattcagtgc agctacatta accaactatg ttctctagtt gaggaacaac taggcctatt 420
tcactgctgt gtagcctcag tgcctaacat gggtgccaaa taaatattng nggattacac 480
tgaattgtaa aaaccattcg tttttgttta caattgccaa aaatctcaaa aggncctgta 540
                                                                   565
tttatgtaat tctttgaaat tatta
<210> 612
<211> 442
<212> DNA
<213> Homo sapiens
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<220>
<221> misc feature
<222> (229)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (253)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (294)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (297)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (319)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (328)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (333)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (365)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (413)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (415)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (440)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (441)
<223> n equals a,t,g, or c
<400> 612
gaccagggtt getecgteeg tgeteegeet egecatgact teetacaget ategecagte 60
gtcggccacg tcgtccttcg gaggcctggg cggcggctcc gtgcgtattg ggccggggt 120
cgcttttcgc gcgcccagca ttcacggggg ctccggcggc cgcggcgtat ccgtgtcctc 180
cgcccgcttt gtgtcctcgt cctcctcggg gggctacggc ggcggctang gcggcgtcct 240
gaccgcgtcc gangggctgc tggcgggcaa cgagaagcta accatgcaga actnaangac 300
cgcttggctt ctactggana agttcgcncc tgnaggggca aagggaacta aaagttaaat 360
ccgcnattgt acaaaacagg gcttggcctt cccggataaa gcattataaa gancntcagg 420
aattggggaa aaattttgn nc
<210> 613
<211> 306
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (5)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (102)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (129)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (172)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (185)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
<222> (190)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (192)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (199)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (213)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (237)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (272)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (299)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (302)
<223> n equals a,t,g, or c
<400> 613
ggcanaggag aactccagga ttgtcctgca gatcgacaac gcccgtttgg ctgcagatga 60
cttccgaacc aagtttgaga cggaacagge tctgcgcatg ancgtggagg ccgacatcaa 120
eggeetgene aggtgetgga tgagetgace etggeecaga acegacettg gngatgeagt 180
tegangeetn angaagagnt ggeetaeeta agnaggaeee tgagggggaa teaattnegt 240
taaggggcca atgggaggcc attaattttg anttggttcc ttccggacct tttggccant 300
cntgtt
                                                                   306
<210> 614
<211> 555
<212> DNA
<213> Homo sapiens
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<220>

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<221> misc feature
<222> (392)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (409)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (433)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (497)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (543)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (545)
<223> n equals a,t,g, or c
<400> 614
ggcgactaca gccactacta cacgaccatc caggacctgc gggacaagat tcttggtgcc 60
accattgaga actccaggat tgtcctgcag atcgacaatg cccgtctggc tgcagatgac 120
ttccgaacca agtttgagac ggaacaggct ctgcgcatga gcgtggaggc cgacatcaac 180
ggcctgcgca gggtgctgga tgagctgacc ctggccagga ccgacctgga gatgcagatc 240
gaaggcctga aggaagagct ggcctacctg aagaagaacc atgaggagga aatcagtacg 300
cttaggggcc aagtgggagg ccaggtcagt gtggaggtgg attccgctcc gggcaccgat 360
ctcgccaaga tcctgagtga catgcgaagc cnatatgagg tcatggccna gcagaaccgg 420
aaggatgett aancetggte accageeegg actgaagaat tgaaceegga ggtegettge 480
cacacggage aacttengat gageaggtee aaggttactg acctgeggeg caaccettaa 540
ggncntgaga atgaa
                                                                   555
<210> 615
<211> 575
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (4)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (28)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (57)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (173)
<223> n equals a,t,g, or c
<400> 615
tganagaaat taaccetcae taaagggnae aaaagetgga geteeacege ggtgegneeg 60
ctctagaact agtggatccc ccgggctgca ggaattcggc acgaggctaa ggctgcgttg 120
gggtgaggcc ctcacttcat ccggcgacta gcaccgcgtc cggcagcgcc agncctacac 180
tegecegege catggeetet gteteegage tegeetgeat etacteggee eteattetge 240
acgacgatga ggtgacagtc acggaggata agatcaatgc cctcattaaa gcagccggtg 300
taaatgttga geetttttgg cetggettgt ttgcaaagge cetggeeaac gtcaacattg 360
ggagceteat etgeaatgta ggggeeggtg gacetgetee ageagetggt getgeaacea 420
gcaggaggtc ctgcccctc cactgctgct gctccagctg aggagaagaa agtggaagca 480
aagaaagaag aatccgagga gtctgatgat gacatgggct ttggtctttt tgactaaacc 540
tcttttataa catgttcaat aaaaagctga acttt
<210> 616
<211> 346
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (117)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (139)
<223> n equals a,t,g, or c
<400> 616
ctcgtgccga attcggcacg agccgccgcc tccgccgcag acgccgccgc gatgcgctac 60
gtcgcctcct acctgctggc tgccctaggg ggcaactcct cccccagcgc caagggnatc 120
aagaagatct tggacaacnt gggtatcgag gcggacgacg accggctcaa caaggttatc 180
agtgagctga atggaaaaaa cattgaagac gtcattgccc agggtattgg caagcttgcc 240
agtgtacctg ctggtggggc tgtagccgtc tctgctgccc caggctctgc agcccctgct 300
gctggttctg cccctgctgc agcagaggag aagaaagatg agaaga
                                                                   346
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<210> 617
<211> 409
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (356)
<223> n equals a,t,g, or c
<220>
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tecegtteeg etgeeegeee tgecaccatg aeggaacagg ceateteett egecaaagae 120
ttettggeeg gaggeatege egeegecate tecaagaegg eegtggetee gategagegg 180
gtcaagctgc tgctgcaggt ccagcacgcc agcaagcaga tcgccgccga caagcagtac 240
aagggcatcg tggactgcat tgtccgcatc cccaaggagc agggcgtgct gtccttctgg 300
aggggcaacc ttgccaacgt cattcgctac ttccccactc aagccctcaa cttcgncttc 360
aaggataagt acaagcagan cttcctgngg ggcgtgnaca agcacacnc
<210> 618
<211> 473
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<213> Homo sapiens
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<222> (446)
<223> n equals a,t,g, or c
<220>
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gagagggggc gactattata caagttggca agttgatcaa agaagctgcc gggaaaagca 120
atctgaagag ggtgaccctg gagcttggag gaaagagccc ttgcattgtg ttagctgatg 180
ccgacttgga caatgctgtt gaatttgcac accatggggt attctaccac cagggccagt 240
nttgtatage egeatneagg atttttgtgg aagaateaat ttatgatgag tttgttegaa 300
ggagtgttga gcgggttaag antatatcct tgggaantcc tttgacccca gnagttcann 360
caagncente agattgacaa ggaccatttg gtaaatactt gaccccattg agagtnggaa 420
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<211> 604
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<222> (371)
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<222> (587)
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<222> (593)
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gaactagtgg atcccccggg ctgcaggaat tcggcacgag gtggtccccc tggcagggac 120
aaatggcgag actaccaccc aagggttgga tgggctgtct gagcgctgtg cccagtacaa 180
gaaggacgga gctgacttcg ccaagtggcg ttgtgtgctg aagattgggg aacacacccc 240
ctcagccctc gccatcatgg aaaatgccaa tgttctggcc cgttatgcca gtatctgcca 300
gcagaatggc attgtgccca tcgtggagcc tgagatcctc cctgatgggg accatgactt 360
gaagcgcttg ncagtatgtg accgaaaagg tgcttggctt gctgctacaa ggctcttgag 420
tgaccaccac atctacctgn aaggcacctt gctgaagccc aacatggtcc cccaggccat 480
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gcttgcactc anaagttttn ttatgaagga gattgcccat ggcgaacccg tctcaancgc 540 tgtgcccgca caantgcccc cccgcttgtc acttgggatc aacnttncct gtnttggaag 600 gcca 604 <210> 620 <211> 312 <212> DNA <213> Homo sapiens <220> <221> misc feature <222> (2) <223> n equals a,t,g, or c<220> <221> misc feature <222> (41) <223> n equals a,t,g, or c <220> <221> misc feature <222> (307) <223> n equals a,t,g, or c <220> <221> misc feature <222> (309) <223> n equals a,t,g, or c<220> <221> misc feature <222> (310) <223> n equals a,t,g, or c <220> <221> misc feature <222> (311) <223> n equals a,t,g, or c <220> <221> misc feature <222> (312) <223> n equals a,t,g, or c <400> 620 gngccaacag ccttgcctgt caaggaaagt acactccgag nggtcaggct ggggctgctg 60 ccagcgagtc cctcttcgtc tctaaccacg cctattaagc ggaggtgttc ccaggctgcc 120 cccaacactc caggecetge ecceteceae tettgaagag gaggeegeet eetegggget 180 ccaggctggc ttgcccgcgc tctttcttcc ctcgtgacag tggtgtgtgg tgtcgtctgt 240 gaatgctaag tccatcaccc tttccggcac actgccaaat aaacagctat ttaaggggga 300

aaaaaanann nn

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ggttgcacga aacacactgg ggaatggagc aaaacagtct ttgaatatcg aacacgcaag 120
gctgtgagac tacctattgt ngatattgca ccctatgaca ttggtggtcc tgatcaagaa 180
tttggtgtgg acntnggncc tgtttgnttt ttataaacca aactctatct gaaatcccaa 240
caaaanaa
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<213> Homo sapiens
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<222> (301)
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (312)
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<223> n equals a,t,g, or c

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gtatgggaaa tgccatgttt gtcaaagagc aactcagtct gctggacagg ttcacggagg 120
atgccaagag gctgtatggc tccgaggcct ttgccactga ctttcaggac tcagctgcag 180
ctaagaagct catcaacgac tacgtgaaga atggaactcg agggactata acctgaacga 240
catacttctc cagctgaagt acacaggcaa tgncagcgna ctnttcatcc tgcctgntca 300
ngncaagatn gnggaagtgg aagccatgtt ggttttcaga gncc
<210> 623
<211> 316
<212> DNA
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<222> (286)
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<222> (294)
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<222> (308)
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<222> (313)
<223> n equals a,t,g, or c
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cggtctgaag ggtctggctg gtgagccagg ttttaaaggc agccgagggg accctgggcc 120
cccaggacca cctcctgtca tcctgccagg aatgaaagac attaaaggag agaaaggaga 180
tgaagggcct atggggctga aaggatacct gggcgcaaaa ggtatccaag gaatgccagg 240
cateceangg etgteaggaa teeetggget geetgggagg eeeggneaca teanaggaat 300
caaggganac atngga
                                                                   316
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<211> 445
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (172)
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<221> misc feature
<222> (311)
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<223> n equals a,t,g, or c

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<222> (327)
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (438)
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ccagggctat gcgccaagac cgtctttaag gcgctccagg cccctgcctt gnacgaagaa 120
catggtgaag gttggcggct acatccttgg ggagtttggg aaacctgaat tntggggacc 180
cccgntncca gcccccagt ggcagttete cctgetecae tncaagttee atetgtgaca 240
ngtggccagg ggncgctgct gctgtnccac ctgacatcaa gttcatcaac ctctttcccc 300
gagaccaagg ncaccatcca gggggtnctg nggggtcggt tttccagttg cgcaatgttg 360
acgtggagtt gcagcaggag ncntggagta acttcacctt cagttcatgg gtcagcaaca 420
agttcnggnc aggtgttnga ggagt
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<211> 401
<212> DNA
<213> Homo sapiens
<220>
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<221> misc feature

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<222> (33)
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<222> (393)
<223> n equals a,t,g, or c
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<222> (397)
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gtgtgatctg accggtcgcg ggggaccagc ccagccctat ttcggctcga gcgaggaact 120
tctgctcccg tgactgaact ctgatcttga tagagagtcc cggccatggc agccaaagga 180
ggcaccgtca aagctgcttc agcattcaat gccactgaag atgcccagac cctgaggaag 240
gccatgaagg ggcttggcac cgacgaagat gccatcatca gcgtcctcgc ctaccgcaac 300
acageceage gecaggaaat caggaeggee ttacaagage accattegge aggggaeett 360
                                                                   401
gtgttaagga acggaccccn ttttgtttnn gantggngtg a
<210> 626
<211> 315
<212> DNA
<213> Homo sapiens
<220>
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<222> (55)
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gctggcacct gggccccccc gggagctggt gctggtggtc cangtgcata accggcccga 120
ataceteana etgetgetgg acteaetteg aaaageeeag ggnaattgae aaegteeteg 180
tcatctttag ccatgacttc tggtcgaccg agatcaatca gctgatcgcc ggggtgaatn 240
tetgteeggt tetgeangtg ttettteett teageattea gttgtteeet aacganttte 300
cangttantg accta
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<210> 627

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<213> Homo sapiens
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<222> (320)
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<222> (327)
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aagtgggatc gagacatgta agcagcatca tggaggtttg aagatgccgc atttggattg 120
gatgaattcc aaattctgct tgcttgcttt ttaatattga tatgcttata cacttacact 180
ttatgcacaa aatgtagggt tataataatg ntaacatgga catgatcttc tttataattc 240
tactttgagt gctgtctcca tgtttgatgt atctgagcag gntgctccac aggtagctct 300
agcagggctg gcaacttann aggtggngag cagagaattc tcttatccaa catcaacatc 360
ttggtcagat ttgaactctt caatctcttg cactcaaagc ttgataagga aa
<210> 628
<211> 577
<212> DNA
<213> Homo sapiens
<220>
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<220>
<221> misc feature
<222> (408)
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<222> (545)
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<222> (560)
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agettaegta egegtgeatg egaegteata getettetat agtgteacet aaatteaatt 120
cactggccgt cgttttacaa cgtcgtgact gggaaaaccc tggcgttacc caacttaatc 180
gccttgcagc acatececet ttegccaget ggcgtaatag cgaagaggcc cgcaccgate 240
gcccttccca acagttgcgc agcctgaatg gcaaatggga cgcgcctgt agcggcgcat 300
taagegegge gggtgtggtg gttacgegea gegtgaeege taeaettgee agegeeetae 360
geceggteet ttegtttett eeetteettt etegeeaegt tegeeggntt teecegtnaa 420
gctntaaatn gggggctncc tttanggttc cgattaangn tttacgggac cttngaccca 480
aaaacttgat tagggtgatg gttacntaat gggccatngc ctgataaacg gttttgccct 540
ttgannttgg agtcccgttn ttaaaaggga ctttggt
                                                                   577
<210> 629
<211> 703
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (146)
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<222> (344)
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<222> (391)
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<222> (414)
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 <223> n equals a,t,g, or c
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 <221> misc feature
 <222> (586)
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<222> (632)
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<222> (651)
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<222> (668)
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cgacgtcata gctcttctat agtgtcacct aaattcaatt cactggccgt cgttttacaa 120
cgtcgtgact gggaaaaccc tggcgntacc caacttaatc gccttgcagc acatccccct 180
ttcgccagct ggcagtaata gcgaagaggc ccgcaccgat cgcccttccc aacagttgcg 240
cagcctgaat ggcgaatggg acgcgccctg tagcggcgca ttaagcgcgg cgggtgtggt 300
ggttacgcgc agcgtgaccg ctacacttgc cagcgcccta gcgnccgctc ctttcgcttt 360
ettecettee tttetegeea egttegeegg nttteeeegt caagetetaa atengggget 420
ccctttangg ttccgatnta gtgctgtacg gcacctngac cccaaaaaac ttgattaggg 480
tgatggttca cgtngtggnc atcgccctga tagacggntt ttcgcccttt gacgttggag 540
nccacqttct taatagtgga ctctttggtc caaacnggan caacantgaa cccctatctc 600
ggnctattct tttgatttat nagggatttt gncgatttca ggnctattgg ntaaaaaatg 660
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547
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ccctggcgtt acccaactta atcgccttgc agnacatccc cntttcgcca gctggcgtaa 240
tagenaaaag geeegnaeeg ategeeette ecaacagttg egeageetga atggeaaatg 300
ggacnenece tgtaneggng cattaanene ggegggtgtg gnggttaeee neanegngae 360
cgctacactt gccagngccc tagcgcccgc tecttteget ttettecett cetttntege 420
cacgttcgcc ggctttcccc gtcaagctnt aaatcggggg ctccctttag ggttccgatt 480
aagngettta egggacettn qneeccaaaa aaacttgatt aggggngatg gnteaengta 540
aaggggccat tgcccttgat aaaacggttn tttngccctt ttgaccttgg aantccccgt 600
                                                            638
ttctttaaaa aangggacct tttggttcna actgggaa
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<211> 187
<212> DNA
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tcgccag
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<213> Homo sapiens
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<222> (23)
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cccgggtcga cccacgcgtc cgactagttc tagatcgcga gcggccgctc tagaggatcc 120
aagettaegt aegegtgeat gegaegteat agetetteta tagtgteace taaatteaat 180
tcactggccg tcgttttaca acgtcgtgac tgggaaaacc ctggcgttac ccaacttaat 240
cgccttgcag cacatccccc tttcgccagc tggcgtaata gcgaagaggc ccgcaccgat 300
cgccc
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<211> 187
<212> DNA
<213> Homo sapiens
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<222> (10)
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<222> (15)
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<222> (180)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (181)
<223> n equals a,t,g, or c
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cgcctgcagg taccggtccg gaattcccgg gtcgacccac gcgtccgaaa aaaaaaaaa 120
aaaaaaaaaa aaaaaaaaaa gggnggacga tctagaggat ccaaagctta cgtacncntn 180
                                                                   187
natgcaa
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<211> 243
<212> DNA
<213> Homo sapiens
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<222> (11)
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<221> misc feature
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<222> (229)
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caggtaccgg tccggaattc ccgggtngac ccacgcgtcc gtggaaatct gtcctccana 120
atccaggcca naaagttcac agtcaaatgg ggaggggtat tcttnatgca ggagacccca 180
ggccctggag gctgcnacat acctnaatcc tgtcccangc cggatcctnc tgaagccctt 240
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ttt

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243
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<211> 180
<212> DNA
<213> Homo sapiens
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gagggggcgg ccgctctaga ggatccaagc ttacgtacgc gtgcatgcga cgtcatagct 120
cttctatagt gtcacctaaa ttcaattcac tggccgtcgt tttacaacgt cgtgactggg 180
<210> 636
<211> 747
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gggtcgaccc acgcgtccgc tagttctaga tcgcgagcgg ccgctctaga ggatccaagc 120
ttacgtacgc gtgcatgcga cgtcatagct cttctatagt gtcacctaaa ttcaattcac 180
tggccgtcgt tttacaacgt cgtgactggg aaaaccctgg cgttacccaa cttaatcgcc 240
ttgcagcaca tccccctttc gccagctggc gtaatagcga agaggcccgc accgatcgcc 300
cttcccaaca gttgcgcagc ctgaatggcg aatgggacgc gccctgtagc ggcgcattaa 360
gegeggeggg tgtggttgtgtt aegegeageg tgaeegetae aettgeeage geeetagege 420
cogeteettt egetttette cetteettte tegecaegtt egeeggettt eecegteaag 480
ctctaaatcg ggggctncct ttagggntcc gatttaagtg ctttacggac ctcgacccca 540
aaaaacttga ttagggtgat gggtcacgta gtgggccatc gcctgataga cggttttcgc 600
ctttgacgtt ggagtcacgt cttaataggg actcttgtnc aaactggaac aacactnaac 660
ctatttggct atcttttgat tataaggatt tgccgattcg gcattggtaa aaatgagtgt 720
tacaaaatta cgcgattaca aaaatan
                                                                   747
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<211> 497
<212> DNA
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<221> misc feature
<222> (463)
<223> n equals a,t,g, or c
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cgccagctgg cgtaatagcg aagaggcccg caccgatcgc ccttcccaac agttgcgcag 240
cctgaatggc gaatgggacg cgccctgtag cggcgcatta agcgcggcgg gtgtggtggt 300
tacgcgcagc gtgaccgcta cacttgccaa gcgccctaag cgcccgttcc tttcgctttc 360
ttcctttctt ttttngccac gttcggccgg cttttccccg taaagcttta aatcnggggg 420
gttcccttaa ggggttccga ttaannggtt ttacgggaac ttngacccca aaaaaacttg 480
attagggggg aaggttn
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<221> misc feature
<222> (385)
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<221> misc feature
<222> (394)
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<221> misc feature
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<223> n equals a,t,g, or c
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<221> misc feature
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<220>
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<222> (496)
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gcgacgtcat agctcttcta tagtgtcacc taaattcaat tcactggccg tcgttttaca 120
acgtcgtgac tgggaaaacc ctggcgttac ccaacttaat cgccttgcag cacatccccc 180
tttcgccagc tggcgtaata gcgaagaggc ccgcaccgat cgcccttccc aacagttgcg 240
cagcctgaat ggcgaatggg acgcgccctg tagcggcgca ttaagcgcgg cgggtgtggt 300
ggttacgegc agcgtgaccg ntacacttgc cagegcccta gcgcccgntc ctttcgcttt 360
cttccttctt tctcggcacg gtcgnccggc tttncccgnc aagctntaaa tcggggggct 420
tccntttagg ggttccgaat taagggcttt accgggaacc ntngaacccc caaaaaactt 480
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<211> 507
<212> DNA
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<221> misc feature
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  <220>
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  <223> n equals a,t,g, or c
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  <222> (356)
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<222> (453)
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acgtcgtgac tgggaaaacc ctggcgttac ccaacttaat cgccttgcag cacatccccc 180
tttcgccagc tggcataata gcgaagaggc ccgnaccgat cgcccttccc aacagttgcg 240
cagcetgaat ggcgaatggg acnegecetg tageggegea ttaagegegg egggtgtngt 300
ggttacgcgc agcgtgaccg ctacacttgc agcnecetag cgcccgctcc tttcnntttn 360
ttnccttcct ttntngcacg tttnacggct ttcccgtcaa gctctanatc gggggctcct 420
ttagggtten atttaatgtt taeggaeett tanceaaaaa aettgatatg gttatggtta 480
ntgtnttgng ccattgcctt atttccc
                                                                   507
<210> 640
<211> 496
<212> DNA
<213> Homo sapiens
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<221> misc feature

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<221> misc feature
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<222> (427)
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<223> n equals a,t,g, or c

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<220>
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<223> n equals a,t,g, or c
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<222> (478)
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cctcaaggtt aaaccctcgg aatacgatag gaaaatgtaa aggccaagat ccaggataag 120
qaaggnattc ctcctgaatn cagcagagaa ctgaatcttt gcctggncaa gcagctggga 180
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aggatgggac gttactttgt gctgaactta caatatttca aaaggggttc ttacttcttn 240
atcttgtgtt gagaatttcg tgggtggtgc ttaggaaagg ggaaggagga agtttttaca 300
accattecea ggaaggntta ggeeeagggn aaagganggt ttaagntggt tgtnenegaa 360
attttttagg gngggttgng attgggcaan tnngtnggct ttggttgggg ggttcccctt 420
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<211> 186
<212> DNA
<213> Homo sapiens
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gcccagtgac accattgaga atgtcaaagc caaaattcaa gacaaggagg gnatcccacc 120
tgaccagcag cgnctgatat ttgccggnaa acagctggaa ggatggncgc aactctntca 180
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gactac
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<221> misc feature
<222> (396)
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<221> misc feature
<222> (405)
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<221> misc feature
<222> (437)
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<220>
<221> misc feature
<222> (494)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (500)
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<223> n equals a,t,g, or c

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gctccgatgt atttgatggt gacctgggaa tggggcagcc aagggctgca aagcctcccc 120
acacatgace ecagecetet acageggtaa ggtgagggac ecacattnee eetgeeetet 180
gagacttngg gggacgttgc cccctgana tgcagnnngg gcctgaatat gtgaaccagc 240
cagatgttcg gccccagccc ccttcgcccc gaagatgngc tngnctgctg cccgacctnc 300
ttggtgccac tctggnaagn ggccaagaat ctnttcccca gggaagaatt gggtcgtcaa 360
aagnggtttt tgcnttttgg gggttccgtt gagaancccg agtangttta caaccccaag 420
ggaagaanet teecetnaag ceecaacett etteettget taageeagee tttgacaace 480
tctaataat't ggancaagan ccaacaaaac cggggggtc
                                                                   519
<210> 643
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<212> DNA
<213> Homo sapiens
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<221> misc feature
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<220>
<221> misc feature
<222> (103)
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 gtgacatcta tnanaggaaa agtgatggca tntatatcat anntctcaag aggacctggg 120
 agaagcttct gctgggca
 <210> 644
 <211> 602
 <212> DNA
 <213> Homo sapiens
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 <221> misc feature
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 <221> misc feature
 <222> (591)
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 <400> 644
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 gcagcatggc tgaccaactg actgaagagc agattgcaga attcaaagaa gctttttcac 120
 tatttgacaa agatggtgat ggaactataa caacaaagga attgggaact gtaatgagat 180
 ctcttgggca gaatcccaca gaagcagagt tacaggacat gattaatgaa gtagatgctg 240
 atggtaatgg cacaattgac ttccctgaat ttctgacaat gatggcaaga aaaatgaaag 300
 acacagacag tgaagaagaa attagagaag cattccgtgt gtttgataag gatggcaatg 360
 gctatattag tgctgcagaa cttcgccatg tgatgacaaa ccttggaaga gaagttaaca 420
 gatgaagaag tttgatgaaa tgatcaggga agcagatatt gatggtgatg gtcaagtaaa 480
 ctatgaagag tttgtaccaa atgatgacag caaaagtgaa agaccttttn ccagaatggg 540
 gttaaatttc ttgnaccaaa antggttaat ttggcctttt ctttggttgg naacttatct 600
                                                                    602
 <210> 645
 <211> 112
 <212> DNA
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<213> Homo sapiens
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<220>
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<222> (24)
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<222> (41)
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<222> (48)
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<222> (59)
<223> n equals a,t,g, or c
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<222> (106)
<223> n equals a,t,g, or c
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atgtgtatgt ccacatacca caccttagga attctcacga aaagtnttcc aa
<210> 646
<211> 514
<212> DNA
<213> Homo sapiens
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<222> (178)
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<221> misc feature
<222> (348)
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<213> Homo sapiens

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<222> (389)
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (444)
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<222> (466)
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<222> (473)
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<220>
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<222> (485)
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ccgtgacaac aacagggtgg gcttcgccga ggctgcccgc ctctagttcc caaggcgtcc 120
gegegecage acagaaacag aggagagtee cagageagga ggeecetgge ccageggnee 180
ctcccacaca cacccacaca ctcgcccgcc cactgtcctg ggcgccctgg aagccggcgg 240
gccaagccga cttgctgttt tgttctgtgg tttcccctcc ctgggttcaa aaatgctgcc 300
tgctgtctgt ctctccatct tgtttggtgg gttaaactga tccaaaanaa aatttgttcc 360
gtgattggaa aaaccaccca acttggaanc nactcttttt cctgggtcct tctctccagg 420
atccccccg gcctacaagc cgtnggttaa cctacccaac agngcncccg gcnccttgaa 480
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<210> 647
<211> 525
<212> DNA
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<213> Homo sapiens

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<222> (11)
<223> n equals a,t,g, or c
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<221> misc feature
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<223> n equals a,t,g, or c
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<222> (23)
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<221> misc feature
<222> (25)
<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (73)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (480)
<223> n equals a,t,g, or c
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<222> (517)
<223> n equals a,t,g, or c
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tggatccccc ggnttgcagg aattcggcac gagcacgcag cggcccgtgg acatcgtctt 120
cctgctggac ggctccgagc ggctgggtga gcagaacttc cacaaggccc ggcgcttcgt 180
ggagcaggtg gcgcggcgc tgacgctggc ccggagggac gacgaccctc tcaacgcacg 240
cgtggcgctg ctgcagtttg gtggccccgg cgagcagcag gtggccttcc cgctgagcca 300
caacctcacg gccatccacg aggcgctgga gaccacgcaa tacctgaact ccttctcgca 360
cgtgggcgca ggcgtggtgc acgccatcaa tgccatcgtg cgcagcccgc gtggcggggc 420
ccqqaqqcac qcaqaqctqc cttcqtqqtc ctcacqqacq qcqtcacqqq caacqacaqn 480
ctgacgagtc ggcgcactcc atgcgcaagc agaacgngga cccac
<210> 648
<211> 317
<212> DNA
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<222> (3)
<223> n equals a,t,g, or c
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<222> (126)
<223> n equals a,t,g, or c
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<221> misc feature
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (176)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (185)
<223> n equals a,t,g, or c
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<220>

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<221> misc feature
<222> (194)
<223> n equals a,t,g, or c
<220>
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<222> (207)
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<222> (245)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (258)
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<221> misc feature
<222> (297)
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<222> (301)
<223> n equals a,t,g, or c
<220>
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<222> (316)
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geneagatgg geatgetgaa ggggeetett ettaacaaat ttetgaceae agecaaagat 60
aagaaccgct gggaggacnc tggtaagcag ctctacaacg tggaggccac atcctatncc 120
ctcttngccc tactgcagct aaaagnettt gactttgtnc ctcccgtcgt nenttngctc 180
aatgnacaga gatnctacgg tggtggntat ggctctaccc aggccacctt catggtgttc 240
caagnettag etcaatanea gaaggaegge eetgaceace aggeactgaa eettgangtg 300
                                                                   317
nacctccaaa tgctcng
<210> 649
<211> 575
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (501)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (509)
<223> n equals a,t,g, or c
<400> 649
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ctttcaaagt tcaccaatac tttaatgtag agcttatcca gcctggagca gtcaaggtct 120
acgcctatta caacctggag gaaagctgta cccggttcta ccatccggaa aaggaggatg 180
gaaagctgaa caagctctgc cgtgatgaac tgtgccgctg tgctgaggag aattgcttca 240
tacaaaagtc ggatgacaag gtcaccctgg aagaacggct ggacaaggcc tgtgagccag 300
gagtggacta tgtgtacaag acccgactgg caaggttcaa gctgtccaat gactttgacc 360
gagtacatca tggccattga gcagaccatc aagtcaggct cggatgaggt gcaggttgga 420
cagcagegea egiteateag ecceateaag tgeagagaag ecctgaaget tgaggagaag 480
aaacactact tcatgtgggg nctcttctnc caattctggg gagagaagcc caaccttagc 540
tacatcatcg ggaaggacac ttgggtggag cactg
                                                                   575
<210> 650
<211> 277
<212> DNA
<213> Homo sapiens
<220>
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<222> (186)
<223> n equals a,t,g, or c
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<222> (265)
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<220>
<221> misc feature
<222> (267)
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<220>
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<222> (269)
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<221> misc feature

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<223> n equals a,t,g, or c
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   agagttaaca gaaggaatag aatgtcttca gacacattcc aagataaatg gcagagattt 120
   gaccttctgg caagaacttg tatccaagtg tttaactgaa tattcatcta agcaaagtgg 180
   ttccanacca aatgttccag aagtttgaaa atggatttgt tcctggacgt actgcacggc 240
   aanctgaagc acaggntact aacgngntna acccanc
   <210> 651
   <211> 357
   <212> DNA
   <213> Homo sapiens
   <220>
   <221> misc feature
   <222> (9)
   <223> n equals a,t,g, or c
   <220>
   <221> misc feature
   <222> (13)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (86)
  <223> n equals a,t,g, or c
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  <222> (89)
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  <220>
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  <222> (97)
  <223> n equals a,t,g, or c
  `<220>
  <221> misc feature
  <222> (100)
  <223> n equals a,t,g, or c
<220>
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<222> (106)
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<220>
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<222> (175)
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<222> (289)
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<222> (324)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (355)
<223> n equals a,t,g, or c
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ttttttctgg gcctggctcg cggcgnacng agatggnagn gcagtnggac gaggccgtga 120
agtaatacac cctaggagga gattcagaag cacaaccaca gcaagagcac ctggnctgat 180
cctgncacca caaggtgtac gaatttgacc aaatttctgg nagaggcatc cctggtgggg 240
gaggaagttt taaggggaac aagcttggag gtgacgctac ttgaggaant tttgagggnt 300
gttcggggca cttttaccag ntgncccaag ggaaaattgt tcccaaaaac atttnca
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<210> 652
<211> 190
<212> DNA
<213> Homo sapiens
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<221> misc feature
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (146)
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<222> (172)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (180)
<223> n equals a,t,g, or c
<400> 652
ggacgctact tcccctatca tagaagagct tatcaccttt catgatcacg ccctcataat 60
cattttcctt atctgcttcc tagtcctgta tgcccttttc ctaacactca caacaaaact 120
aactaatact aacatctnag acgctnanga aatagaaacc gtctgaacta tnctgcccgn 180
catcatccta
<210> 653
<211> 603
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (415)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (600)
<223> n equals a,t,g, or c
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gtcaccctga agtttatatt cttatcctac caggcttcgg aataatctcc catattgtaa 120
cttactactc cggaaaaaaa gaaccatttg gatacatagg tatggtctga gctatgatat 180
caattggctt cctagggttt atcgtgtgag cacaccatat atttacagta ggaatagacg 240
tagacacacg agcatatttc acctccgcta ccataatcat cgctatcccc accggcgtca 300
aaqtatttaq ctqactcqcc acactccacg gaagcaatat gaaatgatct gctgcagtgc 360
totgagocot aggattoato tttottttoa cogtaggtgg cotgactggc attgnattag 420
caaactcatc actagacatc gtactacacg acacgtacta ccgttgtagc ccacttccac 480
tatgtcctat caataggagc tggatttgcc atcataggaa ggcttcattc actgatttcc 540
ctattctcag gctacaccct agaccaaacc tacgccaaaa atcatttcac tatcataatn 600
cac
<210> 654
<211> 356
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (198)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (270)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (302)
<223> n equals a,t,g, or c
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<222> (328)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (340)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (347)
<223> n equals a,t,g, or c
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ggtttttttc ttcgcaggat ttttctgagc cttttaccac tccagcctag cccctacccc 60
ccaattagga gggcactggc ccccaacagg catcaccccg ctaaatcccc tagaagtccc 120
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actcctaaac acatccgtat tactcgcatc aggagtatca atcacctgag ctcaccatag 180
tctaatagaa aacaaccnaa accaaataat tcaagcactg cttattacaa ttttactggg 240
tetetatttt accetectae aaageetean agtaettega gtetecette accattteeg 300
anggcatcta cggctcaaca tttttgnag cccaggcttn cacgganttt cacgtc
<210> 655
<211> 682
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (660)
<223> n equals a,t,g, or c
<400> 655
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gatcacgecc tcataatcat tttccttatc tgcttcctag tcctgtatgc ccttttccta 120
acacteacaa caaaactaac taatactaac ateteagaeg eteaggaaat agaaacegte 180
tgaactatcc tgcccgccat catcctagtc ctcatcgccc tcccatccct acgcatcctt 240
tacataacag acgaggtcaa cgatccctcc cttaccatca aatcaattgg ccaccaatgg 300
tactgaacct acgagtacac cgactacggc ggactaatct tcaactccta catacttccc 360
ccattattcc tagaaccagg cgacctgcga ctccttgacg ttgacaatcg agtagtactc 420
ccqattqaaq ccccattcq tataataatt acatcacaag acqtcttqca ctcatqaqct 480
gtccccacat taggcttaaa aacagatgca attcccggac gtctaaacca aaccactttc 540
accgctacac gaccgggggt atactacggt caatgctctg aaatctgtgg agcaaaccac 600
agtttcatgc ccatcggcct agaattaatt cccctaaaaa tctttgaaat aagggcccgn 660
atttacccta tagcacccct ct
<210> 656
<211> 520
<212> DNA
<213> Homo sapiens
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 tagtcctgta tgcccttttc ctaacactca caacaaaact aactaatact aacatctcag 120
 acgctcagga aatagaaacc gtctgaacta tcctgcccgc catcatccta gtcctcatcg 180
 ccctcccatc cctacgcatc ctttacataa cagacgaggt caacgatccc tcccttacca 240
 tcaaatcaat tggcaccaat ggtactgaac ctacgagtac accgactacg gcggactaat 300
 cttcaactcc tacatacttc ccccattatt cctagaacca ggcgacctgc gactccttga 360
 cggtgacaat cgagtagtac tcccgattga agccccattc gtataataat tacatcacaa 420
 gacgettgna eteaagaget gneecacant aggettaaaa acaggatgea attteeggge 480
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 tgatgattga ctcccagaat tcgaaagaaa ctgagtccca caaagctctg tctgatctgg 120
 agetegeage ceagteaata atetteattt ttgetggeta tgaaaceace ageagtgtte 180
 tttccttcac tttatatgaa ctggccactc accctgatgt ccagcanaaa ctgcaaaagg 240
 gagattgatg cagttttgcc caataaggca ccacctacct atgatgccgt ggtacagatg 300
 gattaccttg acatggtggt gaatgaaacc tcaaattatn cccgttggta tta
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 <212> DNA
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<223> n equals a,t,g, or c

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caggcageca agacccctec caetteette tttggcetee eteteeteag gtatgaaaat 120
gaagctggcc ctgcgcccag gcgtttgaag gctgacatca acggcttgcg ccgagtcctg 180
ggatgagetg accetggeea ggnetgacet ggagntgeag atcgagggee tgaatgaggn 240
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<221> misc feature

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ctaccatgtc catcaaggtg acccagaagt cctacaaggn gtccacctct agcccccggg 120
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cetteageag eegeteetae acgaatngge eeggtteeeg cateaacnee teganettet 180
cccgaatagg cagcagcaac tntngcagtg gcctgggcgg cggctatngt ggggccagcn 240
gcatggnagg catcaccgca gttacggtca accagagcct gctgancccc cttntcctgg 300
aggtggaccc caacatccag gccgtgcgca cccaggagaa ggagcagatc aanaccctca 360
acaacaagtt tgcctcttca tagacaaggt aggttcctgg agcagcagaa caagatgttg 420
gaaaccaagt agagctcctt gagcnnn
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<223> n equals a,t,g, or c

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agtagaacgn gancetecag gntgenatge aagtntgteg caatgttete etgggaceet 120
nagctggtgc nagggggtgg ggcntccaaa atggctgtgg cccatgcntt ganagaaaaa 180
tccanggcca tggactggtg tgggaacaat ggccatacag ggctgttgnc cagggcccta 240
naggttcatt cctcgtnacc ctggatccan aaactgtggg gggncagcca ccatt
<210> 661
<211> 212
<212> DNA
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<222> (207)
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<222> (210)
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ctcatcacca acgatgaggc atacgctgag gagtttggca acgagacgtg gggcgtaaca 120
aaggcagcag agaaacaaat gaaggacaaa caggacgagg agcagaggct taaggaggag 180
gaagaagaca agaacgcaa agaggangan ga
                                                                   212
<210> 662
<211> 130
<212> DNA
<213> Homo sapiens
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<222> (13)
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<223> n equals a,t,g, or c
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<221> misc feature
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<223> n equals a,t,g, or c

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cctgggctgg accntttcat cagacaggct tattagactc tatgctagaa catgaagctt 120
atnggatcng
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<222> (216) ·
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tatctccaag aatgggcaga cccgagagca tgcccttctg gcttacacac tgggtgtgaa 120
acaactaatt gtcggtgnna acaaaatgga ttccactgag ccaccctaca gccagaagag 180
atatgaggaa attgntaagg aagtnagcac ttaccnttaa gaaaaaactg gg
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<212> DNA
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<222> (292)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (294)
<223> n equals a,t,g, or c
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ggacaaattg taggtggccc ctgcagcgcc tgccgccccg gggactcgca gcacccacag 120
caccacgtcc cgaattctca gacgacacct ggagactgtc ccgacactcc cctgagaggt 180
ttctggggcc cgctgcggtc acgaggggg gcccggttac ccaattcgtc ctatagtgat 240
natttacaat tcactggncg tcgttttaca agtcgtgtnt gagttttttt tntntt
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<211> 376
<212> DNA
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aagccaaaat gggaaaggaa aagactcata tcaacattgt cgtcattgga cacgtagatt 120
cgggcaagtc caccactact ggccatctga tctataaatg cggtggcatc gacaaaagaa 180
ccattgaaaa atttgagaag gaggctgctg agatgggaaa gggctccttc aagtatgcct 240
gggtcttgga taaactgaaa gctgagcgtg aacgtggtat cnccattgga tatctccttg 300
tggaaatttg agaccagcaa gtactatgtg actnnncatt gnatgccccc aggacacaga 360
gactttatcc agaaac
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<210> 666
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<212> DNA
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cgaccgcteg cagegetete ttgaccacta tgageeteet gtecageege geggeeegtg 120
tecceggtee ttegagetee ttgtgegege tgttggtget getgetgetg etgaegeage 180
cagggeecat egecageget ggteetgeeg ntgetgtgtt ganagagetg egttgeegtt 240
tgtttacaga ccacgcaagg agtccatccc aaaaatgatc agtaatntgc aagtgtncgc 300
cataggeeca acagtgetee aangngggaa gn
<210> 667
<211> 361
<212> DNA
<213> Homo sapiens
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 taggetgeag accteacecg naccgateca gancactect eccaaggaca ettgtagece 120
 gganctgntc atgtccttgn atccanacaa attgtgccga cgacgccatg gaccctggta 180
 ctaaaganag agcttgttgc gcatttggaa ttgcaccatg cacgggcctg accttctggg 240
 naccccagct gtgtaggcag aggacagggt gacaattttg tctttgcgca tggcntaatg 300
 ccatctgtgg tcatgacagg ttgttcatca agtnnggant caggcaatga aggcngtggg 360
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 <212> DNA
 <213> Homo sapiens
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 <222> (274)
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<222> (455)
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<222> (513)
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aagcatgagc ggatgaaggt ctatgtgccc actggcttct ctgccttccc ttttgagcta 120
ttgcacacgc ctgaaaagtg ggtgaggttc aagtacccaa agctcatctc ctattcctac 180
atggttcgtg ggggccactt tgcggccttt gaggagccgg agctgctcgc ccaggacatc 240
egeaagttee tgteggtget ggageggeat gnanecacce eteteceece gettgecact 300
tecceccaca atgeceteca ggntttettg ggggaagata acentttetg aggatgantt 360
tgcctccgtc ccntgnccag ttggganccc agttcaaccc ctnaaccttc nagttaattc 420
ccaaccccaa tcgtgtggta agcaangggt ttgangataa agatttaatc taaaaaaaaa 480
aaaaaaaatc nggggggggc ccgtaacaat tgnccnaa
                                                                   518
<210> 669
<211> 545
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (8)
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<222> (11)
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<222> (13)
<223> n equals a,t,g, or c
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<222> (58)
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<222> (337)
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<222> (453)
<223> n equals a,t,g, or c
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gccgctctag aactagtgga tcccccgggc tgcaggaatt cggcacgaga gatagaggag 120
gcttccctcc aagaggaccc cggggttccc gagggaaccc ctctggagga ggaaacgtcc 180
agcaccgage tggagactgg cagtgteeca atcetteaat tggtgattte tgetgtgatg 240
taattgtatg caggggttgt ggaaaccaga acttcgcctg gagaacagag tgcaaccagt 300
gtggtgatcg tggcagaggt ggccctggtg gcatgcnggg aggaagaggt ggcctcatgg 360
atcgtggtgg tcccggtgga atgttcagag gtggccgtgg tggagacaga ggtggcttcc 420
gtggtggccg gggcatggac cgaggtggct ttngtggagg aagacgaggt ggccctgggg 480
ggcccctgga cctttgatgg aacagatggg aggaagaaga ggaggacgtg gaggacctgg 540
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                                                                   545
<210> 670
<211> 386
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (141)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (173)
<223> n equals a,t,g, or c
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<222> (192)
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gctacagtca acatettgat ntcactgtgc caactgcggt gcctgccctt canagccctg 180
caetttgttt tnteccetgg cttcatenae tacatcagtg geacecetea tgetetgatt 240
gtgcgtcgct acctctccct gctggacacg gccgtggagc tgganctccc aagataccgg 300
ggtccccgcc ttccccgaan gcagtaagtg cccatctttc cccaacctct cntcaccgac 360
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gtgtggccct gatggtgctc tgtgagaccc accgcgcccg catggtcaaa caccactgct 240
gcccgggctg cggctacttc tgcacggcgg gcaccttcct ggagtgccac cctgacttcc 300
gtgtggccca ccgcttccac aaggcctgtg tgtctcagct gaatgggatg gtcttctgtc 360
cccactgtgg ggaggatact tctgaagctc aagangtgac catccccggg gtgacggggt 420
gacccaacgg ccggca
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tttngacctg agaacagctt cctatgntaa tgccattgng aangtcttca aagtgtacan 180
tgaagetggt gtgacettca catngatgga neatggetga ettneneact atectettca 240
catgtaactt ntgcagacct atcanaagtt tacatgtaac cacagnnntc cctttctctn 300
ctgactnatt aataatggct accattctta acangttaat ccaagtncag cncgtttaag 360
ggngnaaagg antcaaggtt nggcgggttc atntncaagn tgcgtgtggn agtagtaatt 420
ctnctgncan cagtgggncc atttttgggt attttnnctn tnaantanan agggctantt 480
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agtactgcgg ceteetetee teteetaace tegetetege ggeetagett taccegeeeg 180
cctgctcggc gaccagaaca ccttccacca tgaccacctc agcaagttcc cacttaaata 240
aaggcatcaa gcaggtgtac atgtccctgc ctcagggtga gaaagtccag gccatgtata 300
tetggatega tggtaetgga gaaggaetge getgeaagae eeggaeeetg gaeagtgage 360
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aaggcgaggt agccctctgt tgattggtgt acggagtgaa cataaacttt ctactgatca 180
catteetata etetacagaa caggeaaaga caagaaagga agetgeaate tetetegngt 240
ggacagcaca acctgccttn tcccggngga agaaaaagca gnggagtatt actttgcttc 300
tgatgcaann gctgcataga acacaccaat cgcgtcatct ttctggaaga tgatgatgtn 360
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cagtneette aageetacaa geeeegagag aatgatgant tggcactgga gaaageegae 120
gtggtgatgg tgactcacca gagcagtgca cggctggctg gagggcgtga ggctctcaga 180
cggggagcga ggctggtttc ctgtgacagc nntgngagtt catttccaac ccagaggtcc 240
gtgacacaga acctgaaggg aagcttcatc gagtgcaaga cttgccaaac tacagctngt 300
gggaacagca agcctnantt ttctnctgna gaaggagttt tcgtgagctg gaagaacaag 360
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ttg
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gctgcagaag gacaagcagg tctaccgggc cacgcaccgc ctgctgctgc tgggtgctgg 120
agaatctggt aaaagcacca ttgtgaagca gatgaggatc ctgcatgtta atgggtttaa 180
tggagacagt gagaaggcaa ccaaagtgca gganatcaaa aacaacctga aagaggcgat 240
tgaaaccatt gtggccgcca tgagcaacct ggtgcccccc gtggagctgg ccaaccccga 300
aaaccagttc agagtggact acatcctgag tgtgatgaac gtgcctgact ttnacttccc 360
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ggatcatcaa cgagcccacg gccgccgcca tcgcctacgg cctggacaga acgggcaagg 120
gggagcgcaa cgtgctcatc tttgacctgg gcgggggcac cttcgacgtg tccatcctga 180
cgatcgacga cggcatcttc gaggtgaagg ccacggncgg ggacacccac ctgggtgggg 240
aggactttga caacaggctg gtgaaccact tcgtggagga gttcaagaga aaacacaaga 300
aggacatcag ccagaacaag cgagccgtga ggcggctgcg caccgctgcg agagggccaa 360
gaggaccctg tcgtccagca cccaggccag cctggagatc gacttccttg ttttgagggc 420
atogactint acacgiticat caccagggeg aaggiticgaa ggagetgige ticegacett 480
gntnccnaaa cacccctggg aaccccgtgg gaaaaaaggc ttnttgcgcc gaaaggccca 540
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                                                                    550
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<223> n equals a,t,g, or c

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atggaggata tggnctacac tggttacaac aactactatg gatatggtga ttatagcaac 180
cagcagagtg gttatgggaa ggtatccagg cgaggtggtc atcaaaatag ctacaaacca 240
tacttaaatt attccatttg caacttatcc ccaacaggtg gtgaagcata ttttnccatt 300
tgaaggttcc tttgaggggg gctccgcccn ggncttaatt ggcnttccaa ctaaattttt 360
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<220>

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tecetggaag etectgeatg geagetetga eagtgaeact gatggtgetg aacteeccae 120
tggctttggc tggggacacc cgaccacgtt tcttggagca ggtnaaacat gaatgtcatt 180
tcttcaacgg gacggaacgg gtgcggttcc tggacanata cttctatcac caagaagaat 240
acqtqcqctt cgacaqcqac qtqqqqqaat accqqqcqqt qacqqanctq qqqcqqccta 300
actccgaata ctggaacagc cagaaagacn cengggacag aagcgggeeg eggtggacac 360
ctactgcaga nacactacgg ggttgggtgn
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<223> n equals a,t,g, or c
<400> 680
anngtcanac ngacagtnac cgtccggatt cccgggtcga cccacgcgtc cgtgaggtta 60
cagattatgc cattgccagg cgcatagtag atttgcattc aagaattgag gaatcaattg 120
nnaatatota tnocotogat gatatoagaa gatatotnon otatgoaaga aagtntaaac 180
ccaagaattc caaagantca gnggacttca ttgtggagca atntaaacat ctccgcccgn 240
aagatgggtt ctggagtagc ccagtcttca tngagggntn cagttgcggc cncattgagg 300
gccttggatc cgtctctctt ggaagccaat ngctccgggt gcc
<210> 681
<211> 523
<212> DNA
<213> Homo sapiens
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (17)
<223> n equals a,t,g, or c
<220>
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613

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<222> (22)
<223> n equals a,t,g, or c
<220>
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<222> (25)
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<222> (72)
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<221> misc feature
<222> (141)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (383)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (442)
<223> n equals a,t,g, or c
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<222> (487)
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<221> misc feature
<222> (500)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (503)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (514)
<223> n equals a,t,g, or c
<400> 681
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natcttccgt gacactnttg anggnacgcc cgcaggtacc cggtccggaa ttcccgggtc 60

614

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. gacccacgcg thogcccaat tttaccaatc tatcacccta tagaagagct aatgttagta 120
 taagtaacat gaaaacattc ncctccgcat aagcctgcgt cagattaaaa cactgaactg 180
 acaattaaca gcccaatatc tacaatcaac caacaagtca ttattaccct cactgtcaac 240
ccaacacagg catgeteata aggaaaggtt aaaaaaaagta aaaggaacte ggcaaatett 300
accocgcetg tttaccaaaa acatcacctc tagcatcacc agtattagag gcaccgcctg 360
cccagtgaca catgtttaac ggncgcggta ccctaaccgt gcaaaggtag cataatcact 420
tggtccttaa ttagggacct gnatgaatgg ctccacgagg gtcagctggc tcttactttt 480
aaccagngaa attgacctgn cgngaagagg cggnatgaca cag
<210> 682
<211> 713
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (423)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (583)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (595)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (605)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (626)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (633)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (640)
<223> n equals a,t,g, or c
<220>
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<221> misc feature

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<222> (646)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (660)
<223> n equals a,t,g, or c
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ggtcaaccca acacaggcat gctcataagg aaaggttaaa aaaagtaaaa ggaactcggc 60
aaatcttacc ccgcctgttt accaaaaaca tcacctctag catcaccagt attagaggca 120
ccgcctgccc agtgacacat gtttaacggc cgcggtaccc taaccgtgca aaggtagcat 180
aatcacttgt toottaaata gggacotgta tgaatggoto cacgagggtt cagotgtoto 240
ttacttttaa ccagtgaaat tgacctgccc gtgaagaggc gggcatgaca cagcaagacg 300
agaagaccct atggagcttt aatttattaa tgcaaacagt acctaacaaa cccacaggtc 360
ctaaactacc aaacctgcat taaaaatttc ggttggggcg acctcggagc agaacccaac 420
ctncgagcag tacatgctaa gacttcacca gtcaaagcga actactatac tcaattgatc 480
caataacttg accaacggaa caagttaccc tagggataac agcgcaatcc tattctagag 540
tccatatcaa caatagggtt tacgaacctc gatgtttgat cangacattc ccatngtgca 600
gcccnctatt taaaaggttc gttggntcac gantaaaggn cctacntgaa ctgagttcan 660
aaccggagta aattccaagg cgggttttta tctaccttaa aattcccccc tgg
<210> 683
<211> 289
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (15)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (28).
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (73)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (80)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (225)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (237)
<223> n equals a,t,g, or c
<220>
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<222> (240)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (252)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (287)
<223> n equals a,t,g, or c
<400> 683
toccontact aaagngaaca aaagctgnag ctccaccgcg gtggcggccg ctctagaact 60
agtggatccc conggctgcn tgaattcggc acgagcggca cgaggccctg cggggtgtac 120
acceccegtt geggeteggg cetgetetge taccegeece gaggggtgga gaageecetg 180
cacacactga tgcacgggca aggcgtgtgc atggagctgg cgganatcga ggccatncan 240
gaaagcctgc anccctctga caaggacgag ggtgaccacc ccaacanca
<210> 684
<211> 464
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (353)
<223> n equals a,t,g, or c
<400> 684
ggangagece agecetggga ttttcaggtg gtttcatttg gtgaacagga etgaacagag 60
agaactcacc atggaatttg ggctgagctg gctttttctt gtggctattt taaaaggtgt 120
```

617

ccagtgtgag gtgcaattgg tggagtctgg gggaggcttg gtacagcctg gggggtccct 180 gagactetee tgtacagtet etggatteae etttegeaae tatgeeatga gttgggteeg 240 ccagggtcca gggaaggggc tggaatgggt ctcagcaatt gacggtagtg gttataacac 300 atactacgag aggtccctgc agggccgctt tagtgtctcc agagacaatt ccnagaacac 360 actatatctg caaatgaaca gcctgggagc cgaggacacg gccatctatt attgtgcgaa 420 gacagaacgt atgggtactg gctggtacgg acgaaatgac tact <210> 685 <211> 545 <212> DNA <213> Homo sapiens <220> <221> misc feature <222> (6) <223> n equals a,t,g, or c <220> <221> misc feature <222> (10) <223> n equals a,t,g, or c <220> <221> misc feature <222> (14) <223> n equals a,t,g, or c <220> <221> misc feature <222> (16) <223> n equals a,t,g, or c <220> <221> misc feature <222> (20) <223> n equals a,t,g, or c <220> <221> misc feature <222> (326) <223> n equals a,t,g, or.c <220> <221> misc feature <222> (428) <223> n equals a,t,g, or c <220> <221> misc feature

<222> (438)

<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (442)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (456)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (457)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (505)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (509)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (536)
<223> n equals a,t,g, or c
<400> 685
attgantccn ttananaccn cctttatacg actcactata gggaaagctg gtacgcctgc 60
aggtaccggt ccggaattcc cgggtcgacc cacgcgtccg gaccgtcacc cctggagaga 120
eggeeteeat eteetgeagg tetagteaga eeeteetgea tgteaatgga cacaactatt 180
tggattggta catgcagaag ccagggcagc ctccacagct cgtggtctat aggggttcca 240
atcgggcctc cggggtccct gacaggttca gtggcggtgg atcaggcaca gattttacac 300
ttagaatcac cacggtggag gctgangatg ttggcgttta ttactgcatg caagctctac 360 .
aaagtccgta cacttttggc caggggacca agctggagat caaacgaact gtgggctgca 420
ccatctgnct tcatcttncc gncatctgat gaacanntga aatctggaac tgcctctggt 480
gggggcctgc tgaataactt ctatnccana gaggcccaaa gtaccagtgg aaaggnggga 540
taacg
                                                                   545
<210> 686
<211> 496
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (358)
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<223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (417)
 <223> n equals a,t,g, or c
<220>
 <221> misc feature
 <222> (460)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (472)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (481)
 <223> n equals a,t,g, or ċ
 <220>
 <221> misc feature
 <222> (488)
 <223> n equals a,t,g, or c
 <400> 686
 ctactaaagg gaacaaaagc tggagctcca ccgcggtggc ggccgctcta gaactagtgg 60
 atccccggg ctgcaggaat tcggcacgag cggctgggcg ctgaggatca gccgcttcct 120
 geotggatte cacagetteg egeogtgtae tgtegeecca teeetgegeg eccageetge 180
 caagcagcgt gccccggttg caggcgtcat gcagcgggcg cgacccacgc tctgggccgc 240
 tgcgctgact ctgctggtgc tgctccgcgg gccgccggtg gcgcgggctg gcgcgagctc 300
 ggggggcttg ggtcccgtgg tgcgctgcga accgtgcgac gcgcgtgcac tggcccantg 360
 egegeettee geeegeegtg tgegeeggaa ettggtgege caageeggge ttgeggntge 420
 tgcctgacgt gcgcactgag cgaagggcca gccgtgcggn atctacaccg ancgctgtgg 480
 nttccggnct tcgttg
                                                                    496
 <210> 687
 <211> 476
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (3)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (7)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (56)
<223> n equals a,t,g, or c
<400> 687
geneganaen aacceteact aaagggaaca aaagetggag etecacegeg gtgegneege 60
tctagaacta gtggatcccc cgggctgcag gaattcggca cgagattgat gacaccaata 120
tcacacgact gcagctggag acagagatcg aggctctcaa ggaggagctg ctcttcatga 180
agaagaacca cgaagaggaa gtaaaaggcc tacaagccca gattgccagc tctgggttga 240
ccgtggaggt agatgcccc aaatctcagg acctcgccaa gatcatggca gacatccggg 300
cccaatatga cgagctggct cggaagaacc gagaggagct agacaagtac tggtctcagc 360
agattgagga gagcaccaca gtggtcacca cacagtctgc tgaggttgga gctgctgaga 420
cgacgeteae agagetgaga egtacagtee agteettgga gategacetg ggaett
<210> 688
<211> 483
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c
<400> 688
anantaaccc tcactaaagg gaacaaaagc tggagctcca ccgcggtgcg gccgctctag 60
aactagtgga tcccccgggc tgcaggaatt cggcacgagc aggttcccgc ccggaagaag 120
cgaccaaagc gcctgaggac cggcaacatg gtgcggtcgg ggaataaggc agctgttgtg 180
ctgtgtatgg acgtgggctt taccatgagt aactccattc ctggtataga atccccattt 240
gaacaagcaa agaaggtgat aaccatgttt gtacagcgac aggtgtttgc tgagaacaag 300
gatgagattg ctttagtcct gtttggtaca gatggcactg acaatcccct ttctggtggg 360
gatcagtatc agaacatcac agtgcacaga catctgatgc taccagattt tgatttgctg 420
gaggacattg aaaagcaaaa tccaaccagg ttctcaacag gctgacttcc tgggatgcac 480
<210> 689
<211> 339
<212> DNA
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<213> Homo sapiens
<220>
<221> misc feature
<222> (109)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (135)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (155)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (236)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (260)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (280)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (289)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (337)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (338)
<223> n equals a,t,g, or c
<400> 689
aggcaggagg aagccgatcg aaaactcaga gaggaggaag agaagaggag gctaaaggaa 60
gagattgaaa ggcgaggagc agaagctgct gagaaacgcc agaagatgnc agaagatggc 120
ttgtcagatg acagnaaacc attcaagtgt ttcantccta aaaggttcat ctcttcaaga 180
```

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tagaagagcg agcagatttt tgattaagtc tgtgcagaaa agcagtggtg ttcaantcga 240
cccttcaagc agcattagtn ttccaagttt gacagcagan tggagcatnt taccatggca 300
tttgagggga ccaaaagcag ccaaaacctt aaaaaanna
<210> 690
<211> 594
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (473)
<223> n equals a,t,g, or c
<400> 690
gntgctttct ccaccagaag ggcacacttt catctaattt ggggtatcac tgagctgaag 60
acaaagagaa gggggagaaa acctagcaga ccaccatgtg ctatgggaag tgtgcacgat 120
gcatcggaca ttctctggtg gggctcgccc tcctgtgcat cgcggctaat attttgcttt 180
actttcccaa tggggaaaca aagtatgcct ccgaaaacca cctcagccgc ttcgtgtggt 240
tcttttctgg catcgtagga ggtggcctgc tgatgctcct gccagcattt gtcttcattg 300
ggctggaaca ggatgactgc tgtggctgct gtggccatga aaactgtggc aaacgatgtg 360
cgatgctttc ttctgtattg gctgctctca ttggaattgc aggatctggc tactgtgtca 420
ttgtggcagc ccttggctta gcagaaggac cactatgtct tgattccctc ggncagtgga 480
actacacctt tgccagcacc gagggccaag taccttctgg ataccttcac atggtccgag 540
tgcactgaac ccaacacatt ggggaatgga atggatetet ggtttetate etet
<210> 691
<211> 538
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c
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<220> .
<221> misc feature
<222> (55)
<223> n equals a,t,g, or c
<400> 691
ganganacna acceteacta aagggaacaa aagetggage tecacegegg tgegneeget 60
ctagaactag tggatccccc gggctgcagg aattcggcac gagcgcatga ctttgtcttc 120
tecgeacgae tgttacagag gtetecagag cettetetet cetgtgcaaa atggcaacte 180
ttaaggaaaa actcattgca ccagttgcgg aagaagaggc aacagttcca aacaataaga 240
tcactgtagt gggtgttgga caagttggta tggcgtgtgc tatcagcatt ctgggaaagt 300
ctctggctga tgaacttgct cttgtggatg ttttggaaga taagcttaaa ggagaaatga 360
tggatctgca gcatgggagc ttatttcttc agacacctaa aattttggca gataaagatt 420
attetgtgae egecaattet aagattgtag tggtaactge aggagteegt cagcaagaag 480
gggagagtcg gctcaatctg gtgcagagaa atgttaatgt cttcaaattc attattcc 538
<210> 692
<211> 201
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (125)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (143)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (161)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (165)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (183)
<223> n equals a,t,g, or c
<400> 692
geteattgee aegegeeece gacgacegee egacgtgeat tecegattee ttttggttee 60
aaqtccaata tggcaactct aaaggatcag ctgatttata atcttctaaa ggaagaacag 120
acconccaga ataagattac agntgttggg gttggtgctg ntggnatggc ctgtgccatc 180
                                                                   201
aanatcttaa tgaaggactt g
```

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<210>. 693
<211> 589
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (23)
<223> n equals a,t,g, or c
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<222> (271)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (312)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (342)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (354)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (377)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (401)
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<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (424)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (437)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (466)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (491)
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<220>
<221> misc feature
<222> (551)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (571)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (572)
<223> n equals a,t,g, or c
<220> \
<221> misc feature
<222> (576)
<223> n equals a,t,g, or c
<400> 693
nncaaaaagt acctaggtga cantatagaa ggtacgcctg caggtaccgg tccggaattc 60
ccggggttgt taacttgttt attgcagctt ataatggtta caaataaagc aatagcatca 120
caaatttcac aaataaagca ttttttcac tgcattctag ttgtggtttg tccaaactca 180
tcaatgtatc ttatcatgtc tggatcgatc ctgcattaat gaacggccaa cgcgcgggga 240
gaggeggttt gegtattgge tggegtaata negaaaagee egeacegate geeetteeca 300
acagttgcgc ancetgaatg gegaatggga egegeeetgt aneggegeat taanegegge 360
gggtgtggtg gttaccncaa cgtgaccgct acacttgcca ncgccctaac gcccgctcct 420
ttenetttet teecetneet tteteeceea egtteegeeg ggtttneece gteaaactet 480
aaatccgggg ntccccttta agggttccca atttaattgc ttaacggcac ctccaacccc 540
aaaaaaactt naataagggg tgaatggttc nnctanttgg gccaccccc
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626

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<210> 694
<211> 386
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (59)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (135)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (149)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (173)
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<220> °
<221> misc feature
<222> (202)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (204)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (244)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (326)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (340)
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<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (369)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (370)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (383)
<223> n equals a,t,g, or c
<400> 694
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gagatetgee etgeeggeea eggetacaee tacgegaget eegacateeg eetgtecatg 120
aggaaagccg aggangaaga actggcaang cccccaaggg agcaagggca gangagcagc 180
tgggcactgc ccgggccaac ananaagcag cccctccggg ttcgtcacgg acacctggct 240
tgangccggg accatccctg acaaggttga ctctcaagct ggccaggtca cgaccagtgt 300
cactcatgca cctgcctggg tcacanggaa atgccacaan cccacccaat gcctgaacag 360
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aagcagtgtc aagacagtaa ggattcaaac catttgccaa aaatgagtct aagtgcattt 120
actetettee tggcattgat tggtggtace agtggccagt actatgatta tgatttteec 180
ctatcaattt atgggcaatc atcaccaaac tgtgcaccag aatgtaactg ncctgaaagc 240
tacccaagtg ccatgtactg tgatgagctg aaattganaa gtgtaccaat ggtgcctcct 300
ggaatcaagt atctttacct taggaataac cagattgacc atattgatga aaaggccttt 360
gagaatgtaa ctgatctgca gtggctcatt ctagatcaca accttctaga aaactccaag 420
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ggaaatgaaa cttctctttg ggactgcaag aactggcaat ggggtggact tacctgtgat 120
cactatgaag aagccaaaat tacctgctca gcccacaggg aacccagact ggttggaggg 180
gacattecet gttetggacg tgttgaagtg aageatggtg acaegtgggg etceatetgt 240
gattcagact tctctctgga agctgccagc gttctatgca gggaattaca gtgtggcaca 300
gttgtctcta tcctgggggg agctcacttt ggagagggaa tggacagatc tgggctgaag 360
aattccagtg ttgagggaca tgaatcccca tctttcatct tnccagtagn aaccccgccc 420
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aaaaggaact tgtagccaca gcaa
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ccagacgaca gggaagaagg agctgcctct acggctgagg aaanagccaa gaaaaaaaga 120
cgaaagaaga agaagagcaa agggccttct gcaggtaaag agagttttat gttttcccag 180
teceeteegg gaacggetga actgtttgge teaggeeegt tgagggggee gggaeegggg 240
ccccagagcc ccgactagac tgattcttgg gcctgacagg gtggcaaagc cgggctatag 300
atcanggtgc acctgagctt tctctgatgt atgcccangc agatctccag gtattcagag 360
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tgcgtgtgat taggg
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ngcacagttt tctctcttgg agcatgcatg gaaggcctga atattttgct taacagactg 120
ttggggattt cattatatgc agagcagcct gcaaaaggag aggtgtggag cgaagatgtc 180
cgaaaactgg ctgttgttca tgaatctgaa ggattgttgg ggtacattta ctgtgatttt 240
tttcagcgag cagacaaacc acatcaggat tgccatttca ctatccgtgg aggcagacta 300
aaaggaagat gggagactat ncaactccca gttgtaagtt cttatgctgg aatcttcccc 360
gttcccgnna gggagttctc caactttggc naangcctgg gcatgatggg aaaacctttc 420
ccagganggg ggac
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 gtaaaatttg gtgcagatgc ccgagcctta atgcttcaag gtgtagacct tttagccgat 180
 gctgtggccg ttacaatggg gccaaaggga agaacagtga ttattgagca gagttgggga 240
 agtcccaaag taacaaaaga tggtgtgact gttgcaaagt caattgactt aaaagataaa 300
 tacaagaaca ttggagctaa acttgttcaa gatgttgcca ataacacaaa tgaagaagct 360
 ggggatggca ctaccactgc tactgtactg gcacgctcta tagccaagga aggcttcgag 420
                                                                    435
 aagattagca aaggt
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 <211> 406
 <212> DNA
 <213> Homo sapiens
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 tcccaaagta acaaaagatg gtgtgactgt tgcaaagtca attgacttaa aagataaata 180
 caagaacatt ggagctaaac ttgttcaaga tgttgccaat aacacaaatg aagaagctgg 240
 ggatggcact accactgcta ctgtactggc acgctctata gccaaggaag gcttcgagaa 300
 qattaqcaaa ggtqctaatc cagtggaaat caggagaggt gtgatgttag ctgttgatgc 360
                                                                    406
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ttca
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geocacetgg teeggegeta cetgggegat geeteggtgg anccegacee cetgeagatg 120
ccaacettee egecagaeta eggetteece gaacgeaagg anegeganat ggtggccaca 180
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cancangana tgatggacgc gcactnaagc tccanctgcg ggantactgc gcccaccaac 240
tcatccgggt gctcaattnc aaccttaaan cttcccccac ttccttggct tgcnaaccag 300
gaacgggaca aatnggaata ntnccaaaca ccccanaant tttnttnccc ttaaanantt 360
tttaaacgga aacgaagggt ntcccccccg gaaaaaaaac nggggnaaaa aaaggggaaa 420
ttttttnccc ccccccgcc cgnggaaatt ttcccccccg tt
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<211> 436
<212> DNA
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ggtgttgcgg ctttataagc gggcgctacg ccacctcgag tcgtggtgcg tccagagaga 120
caaataccga tactttgctt gtttgatgag agcccggttt gaagaacata agaatgaaaa 180
ggatatggcg aaggccaccc agctgctgaa ggaggccgag gaagaattct ggtaccgtca 240
gcatccacag ccatacatct tecetgacte teetgggggc acetectatg agagatacga 300
ttgctacaag gtcccagaat ggtgcttaga tgactggcat ccttctgaga aggcaatgta 360
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agngcctgcg tncgtgagaa ttcagcatgg aatgactcta ctatttnctg ggatttctgn 120
tnctggntgn aagattgcca cttgatgccg ccaaacgatt ncatgatgag ctgggnaatg 180
aaagaccttn tgcttacatg anggagcaca atcaattaaa tggctggtnt tctgatgaaa 240
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tgctggaagg gaggcccgtg tgcaaggcgg tcctgaccag ngactnacca acccttggng 360
qqctcaaata naacattngc cggngaacct gatattccct aaangccaaa aggaagaagc 420
caatggcaac ataggctatg anaagaactg ganaaatgaa gctgggntaa acagctgaac 480
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canaagg
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tgccgccacc cgatggaaga ttcgatggac atggacatga gccccctgag gccccagaac 120
tatcttttcg gttgtgaact aaaggccgac aaagattatc actttaaggt ggataatnat 180
gaaaatgagc accagttatc tttaagaacg gtcngtttng gggctggtgc aaaggatgag 240
ttgcacattg ttgaagcaga ggcaatgaat tacgaaggca gtccaattaa agtaacactg 300
gcaactttga aaatgtctgt acagccaacg gttttcccct tgggggcttt gaataacacc 360
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<211> 360
<212> DNA
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<222> (335)
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<222> (343)
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<223> n equals a,t,g, or c
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<222> (355)
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gegegeetee teegeegeeg eggaeteegg eagetttate geeagagtee etgaactete 120
getttettt taateeestg categgatea eeggegtgee eeaccatgte agaegeagee 180
gtagacacca gctccgaaat caccaccaag gacttaaagg agaagaagga agttgtggaa 240
gaggcagaaa tggaagagac gccctgctaa cgggatgcta atgaggnaat ggggagcagg 300
aggtgacatg aggtagccga gaagaggaag aagtngggag aanagagaga anaanaagtt 360
<210> 709
<211> 253
<212> DNA
<213> Homo sapiens
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<222> (17)
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ggcccaccat cccggcgngg accttttccg ttagcgtggg tgatattgtt cctgctcgag 180
geneaaatng gteettggna teteetteea tetgeecatt aactetegea agtgeeteeg 240
ngaggaaatt cnc
                                                                   253
<210> 710
<211> 496
<212> DNA
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<220>
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<221> misc feature

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<222> (469)
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<220>
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<222> (476)

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<220>
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caatgatgct tttaagggaa tgactagtga agaaaaagaa attctgatac gggacaaaaa 120
tgctcttcaa aacatcattc tttatcacct acaccaggag ttttcattgg aaaaggattt 180
gaacctggtg ttactaacat ttttaaagac cacacaaggn agcaaaatct ttctggaagg 240
aagtgaaatg gttacacttc tggtgaatgg atttggaaat ccaaaagant ctgacatcca 300
tggnccacca anggtggtaa tttcatgttg taggttaaac tncncttttc cagcagncac 360
accttttggg natggntcaa ctggtnggga tacttgatta tttnatncaa tnncctcccn 420
atttaaggtt ttttccgggg tgggccctt caagggaatn ccngggctnt tttttnacac 480
ctnaattttt tcccc
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<210> 711
<211> 461
<212> DNA
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<222> (12)
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<222> (37)
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<221> misc feature
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ttncccgggc tgcaggaatt cgcacgagg tcgcagacac tatgctgcct cccatggccc 120
tgcccagtgt atcttggatg ctgctttcct gcctcatgct gctgtctcag gttcaaggtg 180
aagaacccca gagggaactg ccctctgcac ggatccgctg ncccaaaggc tccaaggcct 240
atggctccca ctgctatgcc ttgtttttgt caccaaaatc ctggacagat gcagatctgg 300
cctgccagaa gcggccctct ggaaacctgg tgtctgngct cagtggggct gagggatcct 360
tegngeetee etggtgaaga geattggtaa eagetaetea taegtetgga ttgggeteea 420
tgaccccaca cagggcaccg agcccaatgg ataaaggttg g
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<211> 392
<212> DNA
<213> Homo sapiens
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<222> (359)
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<222> (368)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (389)
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tggtctcggg gacctccgca gcagctcccc agggcccacg ggccagcccc gccgccctcg 180
caacctggca gccgccgccg tggaagagca gtatagctgt gactatggat ctggcagatt 240
ctttatcctt tgtggacttg gaggaattat tagctgtggc acaacacata cagcattggt 300
tcctctagat ctggttaaat gcagangcag gtttgttttt gcatgctgga cttagagcna 360
ttgaagcntg actgangtta agtattagna ta
<210> 713
<211> 734
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (256)
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<222> (496)
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<222> (580)
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<222> (601)
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<222> (642)
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<220>
<221> misc feature
<222> (690)
<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (703)
<223> n equals a,t,g, or c
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aggatcacca gataccaggg tgttaatctt tatgtgaaaa atcttgatga tggtattgat 120
gatgaacgtc tccggaaaga gttttctcca tttggtacaa tcactagtgc aaaggttatg 180
atggagggtg gtcgcagcaa agggtttggt tttgtatgtt tctcctcccc agaanaagcc 240
actaaagcag ttacanaaat gaacggtaga attgtggcca caaagccatt gtatgtagct 300
ttagctcagc gcaaagaaga gcgccaggct cacctcacta accagtatat gcagagaatg 360
gcaagtgtac ganctgttcc caaccctgta atcaacccct accagccagc acctccttca 420
ggttacttca tggcagctat cccacagact cagaacgtgc tgcatactat cctcctagcc 480
aaattgctca actaanacca agtcctcgct ggactgctca gggtgccata actcatccat 540
tccaaaatat gcccggtgct atccgcccag ctgctcctan aacaccattt agtactatga 600
naacagette tteteageaa catettaatg cacagecaca anttacaatg cacancetge 660
tgttcatgtt caaggtcagg aacctttgan tgcttccatg ttngcatctg ccccccccca 720
aaacaaaacc aatt
                                                                   734
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tctagcaact agtggatccc ccgggcctgt caggaattcg gcacgagctg ggacaagcga 120
gtttttaaac aaagtgactg aggcacagga agatggccag tcaacttctg aattgattgg 180
ccagtttggt gtcggtttct attccgcctt ccttgtagca gataaggtta ttgtcacttc 240
aaaacacaac aacgataccc agcacatctg ggagtctgac tccaatgaat tttctgtaat 300
tgctgaccca agaggaaaca ctctaggacg gggaacgaca attacccttg tcttaaaaga 360
agaagcatct gattaccttg aattggatac aattaaaaat ctcgtcaaaa aatattcaca 420
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<222> (271)

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gttcataaac tttcctattt atgtatggng cagcaagact gaaactgttn aggagcccat 480
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<212> DNA
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<220>
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<222> (116)
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<221> misc feature
<222> (250)
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<222> (326)
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<222> (339)
<223> n equals a,t,g, or c
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653

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anaantacaa caagtgggaa acgatagagg cttggactca acaagtcgcc actganaatc 120
cagocotoat ototogoagt gttatoggaa coacatttga gggacgeget atttacotoc 180
tgaaggttgg caaagctgga caaaataagc ctgccatttt catggactgt gggtttccca 240
tgccaganan ttggatttct ccctgcattc ngccagtngg ttttntaaaa aangcggttc 300
ccttcctatn gacntttana ncccanttga caaacttcnc caacaattta aanttttatn 360
ttcccgccct gtggccccaa tattgaaggg caacttcnac cccgggaacn aaaacccaat 420
tntggaaaaa aaaacccccc cccccctgg tgggattctt gctttggttg ggnnccaccc 480
caaaaaaatt t
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<212> DNA
<213> Homo sapiens
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<221> misc feature
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 <222> (303)
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<223> n equals a,t,g, or c
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<222> (326)
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gctacccggt gtgcggcagc gacggcacca cctacccgag cggctgccag ctgcgcgcg 120
ccagccagag ggccgagagc cgcggggaga aggccatcac ccaggtcagc aagggcacct 180
gcgagcaagg tccttccata gtgacgcccc ccaaggacat ctggaatgtc actggtgccc 240
angtgtactt gagctgtgag gtcatcggaa tcccgacacc tgtcctcatc tggaacaagg 300
tanaaagggg tcactatgga nntcanagga c
                                                                    331
<210> 717
<211> 486
<212> DNA
<213> Homo sapiens
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<222> (25)
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<220>
<221> misc feature
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ctagtggntc ccccgggnct gcaggaattc ggcacgagna tattagncag cggttattcg 120
gtgagcggtg gtggtttatt cttccgtgga gttaagggct ccgtggacat ctcaggtctt 180
cagggtette catetggaac tatataaagt teagaaaaca tgtetegaga tatgaeteea 240
ggaccactat attitctcca gaaggtcgct tataccaagt tgaatatgcc atggaagcta 300
ttggacatgc aggcacctgt ttgggaattt tagcaaatga tggtgttttg cttgcagcag 360
agagacgcaa catccacaag cttcttgatg aagtcttttt ttctgaaaaa atttataaac 420
tcaatgagga catggcttgc agtgtggcag gcataacttt ctgatgctaa tgttctgact 480
aatgac
                                                                   486
<210> 718
<211> 479
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (436)
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<400> 718
tegacecacg egteegeage ceaeceatee aegttgaete ateeteagag aegaategae 60
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acceteaact cagatggata cacceetgag ecagacaaac egeggeegat geecatggae 120
acqagcqtqt atqaqaqccc ctacaqcqac ccaqaqqaqc tcaaqqacaa qaaqctcttc 180
ctgaagcgcg ataacctcct catagctgac attgaacttg gctgcggcaa ctttggctca 240
gtgcgccagg gcgtgtaccg catgcgcaag aagcagatcg acgtggccat caaggtgctg 300
aagcagggca cggagaaggc agacacggaa gagatgatgc gcgaggcgca gatcatgcac 360
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<211> 572
<212> DNA
<213> Homo sapiens
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gatgattgtc atagaactgg gcaccaatcc gctgaagagc tcaggaattg aaaatggggc 120
```

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tttccaggga atgaagaagc tctcctacat ccgcattgct gataccaata tcaccagcat 180
 tcctcaaggt cttcctcctt cccttacgga attacatctt gatggcaaca aaatcagcag 240
 agttgatgca gctagcctga aaggactgaa taatttggct aagttgggat tgagtttcaa 300
cagcatetet getgttgaca atggetetet ggecaacaeg ceteatetga gggagettea 360
cttggacaac aacaagctta ccagagtacc tggtgggctg cagagcataa agtacatnca 420
nggtggctac cttcataaca accatatctc tgtagttgga tcaaagtgac ttctggccac 480
ctggacacaa ccacccaaaa ngnttcttaa ttccgggtgg gaagentttt aacaaacccg 540 -
ggccangact ggggagaana cagccatcca cc
<210> 720
<211> 487
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<222> (468)
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tgtcagtgta tagagggttc tttggatgta gacacttttc aaagaccaat gagctgctgc 180
agaagtetqq caagaageee attgactqqa aggagetgtg atcateaget gaggggtgge 240
ctttgagaag ctgctgttaa cgtatttgcc agttacgaag ttccactgaa aattttccta 300
ttaattetta agtaetetge ataaggggga aaagetteea gaaageagee atgaaceagg 360
ctgtccagga atggancctg tatccaacca caaacaacaa aggctaccct ttgacccaaa 420
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acttaat
<210> 721
<211> 464
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (312)
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<222> (448)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (455)
<223> n equals a,t,g, or c
<400> 721
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tectgggttg tgaggagteg eegetgeege eactgeetgt getteatgag gaagatgete 120
geogeogtet coegegtget gtetggeget tetcagaage eggeaageag agtgetggta 180
gcatcccgta attttgcaaa tgatgctaca tttgaaatta anaaatgtga ccttcaccgg 240
ctggaagaag ccctcctgtc acaacagtgc tcaccaaggg aagatgggct caaatactac 300
aggatgatgc anactgtacc cgaatggaat tgaaacagat cactgtntna acagaaaatt 360
atcntggttt ctgtccttgt gtgatgtcag aacttgctgt gtggcctgga gccgnatcac 420
cccaaacact ctccanctac ggntccgntt atttnccggg cttc
<210> 722
<211> 320
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (12)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (43)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (113)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (142)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (152)
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WO 00/55350

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<223> n equals a,t,g, or c
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<222> (182)
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<222> (211)
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<222> (263)
<223> n equals a,t,g, or c
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<222> (275)
<223> n equals a,t,g, or c
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<222> (281)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (299)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (308)
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gttgcacagc anctgcacgc gccgtggctc cggatctctt cgnctttgca gcgtagcccg 60
agteggteag egeeggatga ceteageage eatgtegaag eeceatagtg aancegggae 120
tgccttcatt cagacccage anctgcacge anneatggct gacacattcc tggagcacat 180
gngccgcctg gacattgatt caccacccat nacaggccgg aacactggca tcatctgtac 240
cattggccca gcttcccgat cangtggaga cggtnaagga natgattaaa gcctggaang 300
aatgtggntc gtctgaactt
                                                                   320
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<210> 723

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<211> 152
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<213> Homo sapiens
<220>
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (87)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (111)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (127)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (148)
<223> n equals a,t,g, or c
<400> 723
gcccaccatg gctgcaatcc gaaagaagct ggtgatcgtt ggggatggtg cctgtgggaa 60
gacctgcctc ctcatcgtnt tcagcangga tcagtttccg gaggtctacg nccctactgt 120
cctttgngaa ctatattgcg cacattgngg cg
                                                                    152 .
<210> 724
<211> 573
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (463)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (514)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (553)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (559)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (569)
<223> n equals a,t,g, or c
<4.00> 724
gctgctatgt tcaatataag aaatattgga aagacgctcg tcaccaggac ccaaggaacc 60
aaaattgcat ctgatggtct caagggtcgt gtgtttgaag tgagtcttgc tgatttgcag 120
aatgatgaag ttgcatttag aaaattcaag ctgattactg aagatgttca gggtaaaaac 180
tgcctgacta acttccatgg catggatctt acccgtgaca aaatgtgttc catggtcaaa 240
aaatggcaga caatgattga agctcacgtt gatgtcaaga ctaccgatgg ttacttgctt 300
cgtctgttct gtgttggttt tactaaaaaa cgcaacaatc agatacggaa gacctcttat 360
gctcagcacc aacaggtccg ccaaatccgg aagaagatga tggaaatcat gacccgagag 420
gtgcagacaa atgacttgaa agaagtggtc aataaattga ttncagacgc attggaaaag 480
acatagaaaa ggcttggcaa tctattatcc tctncatgat ggcttcgtta gaaaagtaaa 540
aatgctgaag aanccaagnt tgaatgggna aac
<210> 725
<211> 403
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c
<400> 725
gettgaaant aacceteact aaagggaaca aaagetggag etecacegeg gtgeggeege 60
tctagaacta gtggatcccc cgggctgcag gaattcggca cgagtcctgg tccgcgccag 120
ageceagege geetegtege catgeetegg aaaattgagg aaatcaagga etteetgete 180
acagcccgac gaaaggatgc caaatctgtc aagatcaaga aaaataagga caacgtgaag 240
tttaaagttc gatgcagcag atacctttac accctggtca tcactgacaa agagaaggca 300
gagaaactga agcagtccct gcccccggt ttggcagtga aggaactgaa atgaaccaga 360
cacactgatt ggaactgtat tatattaaaa tactaaaaat cct
                                                                   403
<210> 726
<211> 502
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<222> (7)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (12)
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<220>
<221> misc feature
<222> (256)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (281)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (380)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (391)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (428)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (456)
<223> n equals a,t,g, or c
<400> 726
cgcaagnncg anactaaccc tcactaaagg gaacaaaagc tggagctcca ccgcggtgcg 60
gccgctctag aactagtgga tcccccgggc tgcaggaatt cggcacgaga gccatcaggt 120
aagccaagat gggtgcatac aagtacatcc aggagctatg gagaaagaag cagtctgatg 180
tcatgcgctt tcttctgagg gtccgctgct ggcagtaccg ccagctctct gctctccaca 240
gggctccccg ccccanccgg cctgataaag cgcgccgact nggctacaag gccaagcaag 300
gttacgttat atataggatt cgtgttcgac gtggtggccg aaaacgccca gttcctaagg 360
gtgcaattac ggcaagcctn tccatcatgg ngttaaccag ctaaagtttg ctcgaagcct 420
```

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teagteentt geagaggage gagetggaeg ceaetntggg getetgagag teetgaatte 480
ttactgggtt ggtgaagatt cc
<210> 727
<211> 361
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (17)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (309)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (318)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (360)
<223> n equals a,t,g, or c
<400> 727
ggcacgagcg aacgcgnaga gcacgccatg aaggcctcgg gcacgctacg agagtacaag 60
gtagtgggtc gctgcctgcc cacccccaaa tgccacacgc cgccctcta ccgcatgcga 120
atctttgcgc ctaatcatgt cgtcgccaag tcccgcttct ggtactttgt atctcagtta 180
aagaagatga agaagtcttc aggggagatt gtctactgtg ggcaggtgtt tgagaagtcc 240
cccctgcggg tgaagaactt cgggatctgg ctgcgctatg actcccggag cggcacccac 300
aacatgtanc gggaatancg ggacctgacc aacgcaggcg ctgtcaacca gtgtaacggn 360
g
<210> 728
<211> 401
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (6) .
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (200)
<223> n equals a,t,g, or c
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<220>

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<220>
<221> misc feature
<222> (234)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (251)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (319)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (332)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (334)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (360)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (389)
<223> n equals a,t,g, or c
<400> 728
gaagangete geetetagtg teeteegetg tggcaagaag aagtetggtt agaceecaat 60
gagaccaatg aaatcgccaa tgccaactcc cgtcagcaga tccggaagct catcaaagat 120
gggctgatca tccgcaagcc tgtgacggtc cattcccggg ctcgatgccg gaaaaacacc 180
ttggcccgcc ggaaaggcan gcacatgggc atagttagcg gaaaggtaca gccnatgccc 240
gaatgccaaa naaggtcaca tggattaaga aaatgaagat tttgcgcccg ctgctcaaaa 300
aatacgtgaa tottaaaana togatogooa entntttoac agootgttoo taaagttaan 360
ggaatttttt caaaaacaac cgattctcnt ggaacacttc c
                                                                   401
<210> 729
<211> 530
<212> DNA
<213> Homo sapiens
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<221> misc feature
 <222> (7)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (10)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (12)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (14)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (60)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (527)
 <223> n equals a,t,g, or c
 <400> 729
 gcacagngan ancnaaccct cactaaaggg aacaaaagct ggagctccac cgcggtgcgn 60
 ccgctctaga actagtggat cccccgggct gcaggaattc ggcacgagcc gccatcttcc 120
 agtaattcgc caaaatgacg aacacaaagg gaaagaggag aggcacccga tatatgttct 180
 ctaggccttt tagaaaacat ggagttgttc ctttggccac atatatgcga atctataaga 240
 aaggtgatat tgtagacatc aagggaatgg gtactgttca aaaaggaatg ccccacaagt 300
gttaccatgg caaaactgga agagtctaca atgttaccca gcatgctgtt ggcattgttg 360
taaacaaaca agttaagggc aagattettg ccaagagaat taatgtgcgt attgagcaca 420
 ttaagcactc taagagccga gatagcttcc tgaaacgtgt gaaggaaaat gatcagaaaa 480
agaaagaagc caaagagaaa ggtacctggg ttcaactaaa gcgccancct
<210> 730
<211> 375
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (33)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
 <222> (55)
 <223> n equals a,t,g, or c
 <220>
<221> misc feature
 <222> (87)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (97)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (111)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (121)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (124)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (125)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (142)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (181)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (183)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (190)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (198)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (206)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (229)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (241)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (248)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (262)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (269)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (284)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (322)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (333)
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<223> n equals a,t,g, or c
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 <221> misc feature
<222> (354)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (367)
<223> n equals a,t,g, or c
<400> 730
gggtggttgc tgccgaaatg ggcaagttca tgnaaccaag aaagtggtgc ttgtnctggc 60
tggacgctac tccggacgca aagctgntca tcgtaanaga acattgaatg ntggcacctc 120
naanngcccc tacagccatg cnctggtggc tgggaattga accgctaccc ccgcaaatga 180
nengetgeen tggggeanga agaagntege caggaggtea aagatatant ettttgtgaa 240
ngtgtgtnac tacaatcacc tnatgcccnc aaggtactct gtgngatatt ccccttgggg 300
caaagctgta cgttcattag gntgtcttcc ganattcctg gctcttaaac gctnggcccg 360
aaggagnccc aggtc
                                                                    375
<210> 731
<211> 207
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (143)
<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (177)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (187)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (201)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (207)
<223> n equals a,t,g, or c
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<400> 731
gcgccgctgc gaagggagcc gccgccatgt ctgcgcatct gcaatggatg gtcgtgcgga 60
actgctccag tttcctgatc aagaggaata agcagaccta cagcactgag cccaataact 120
tgaaggcccg caattccttc cgntacaacg gactgattca ccgcaagact gtgggcntgg 180
agccggnagc cgacggcaaa ngtgtcn
<210> 732
<211> 702
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (620)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (628)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (655)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (686)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (690)
<223> n equals a,t,g, or c
<400> 732
ggcagaatgn ctcccgcaaa gaagggtggc gagaagaaaa agggccgttc tgccatcaac 60
gaagtggtaa cccgagaata caccatcaac attcacaagc gcatccatgg agtgggcttc 120
aagaagcgtg cacctcgggc actcaaagag attcggaaat ttgccatgaa ggagatggga 180
actccagatg tgcgcattga caccaggctc aacaaagctg tctgggccaa aggaataagg 240
aatgtgccat accgaatccg tgtgcggctg tccagaaaac gtaatgagga tgaagattca 300
ccaaataagc tatatacttt ggttacctat gtacctgtta ccactttcaa aaatctacag 360
acagtcaatg tggatgagaa ctaatcgctg atcgtcagat caaataaagt tataaaattg 420
caaaaaaaa aaaaaagggc ggccgctcta gaggatccaa gcttacgtac gcgtgcatgc 480
```

<221> misc feature

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tcgtgactgg gaaaaccctg cgttacccaa cttaatcgcc ttgcagcaca tcccctttcg 600
 ccagctgcgt aataacgaan aggcccgnac cgatcgcctt tccacagttg cgcancctga 660
 atggcgaatg gacgcgcctt taccgngcan taagcgccgc gg
<210> 733
 <211> 441
 <212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (22)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (62)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (99)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (101)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (118)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (126)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (152)
<223> n equals a,t,g, or c
<220>
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<222> (185)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (212)
<223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (260)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (310)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (356)
 <223> n equals a,t,g, or c
 <400> 733
 naattaaccc tcactaaagg gngcaaaagc tggtgctcca ccgcggtgcg accgctctag 60
 anctagtggt tececeggge tgeaggattt eggeaegane negtgeagat tegageanag 120
 gagcgnaagg gaacgtcatc gtttggaaag cntcgcaata agacgcacac gttgtgccgc 180
 cgctntggct ctaaggccta ccaccttcag angtcgacct gtggcaaatt tggctaccct 240
 gccaagcgca agagaaagtn taactggagt gccaaggcta aaagacgaaa taccaccgga 300
 actggtcgan tgaggcacct aaaatttgta taccgcagat tcaggcatgg tttccntgaa 360
 ggaacaacac ctaaacccaa gagggcagct gttgcagcat ccagttcatc ttaagattgt 420
 caacgattag tcatgcaata a
 <210> 734
 <211> 379
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (42)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (323)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (324)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (342)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (346)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (375)
<223> n equals a,t,g, or c
<400> 734
ggccgcagaa gcgagatgac gaagggaacg tcatcgtttg gnaagcgtcg caataagacg 60
cacacgttgt gccgccgctg tggctctaag gcctaccacc ttcagaagtc gacctgtggc 120
aaatgtggct accctgccaa gcgcaagaga aagtataact ggagtgccaa ggctaaaaga 180
cgaaatacca ccggaactgg tcgaatgagg cacctaaaaa ttgtataccg cagattcagg 240
catggattcc gtgaaggaac aacacctaaa cccaagaggg cagctgttgc agcattccag 300
ttcatcttta agaatgtcaa cgnntttagt catgcaataa antgtnctgg ggttttaaaa 360
aattaaaaga aaagnaaaa
                                                                   379
<210> 735
<211> 187
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (172)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (176)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (177)
<223> n equals a,t,g, or \c
<220>
<221> misc feature
<222> (179)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (185)
<223> n equals a,t,g, or c
<400> 735
gegggategt eggtaaatae gggaceeget atggggeete eeteeggaaa atggtgaaga 60
aaattgaaat cagccagcac gccaagtaca cttgctcttt ctgtggcaaa accaagatga 120
agagacgagc tgtggggatc tggcactgtg gttcctgcat gaagacagtg gntggnngng 180
cctgnac
<210> 736
<211> 576
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (94)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (334)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (340)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (361)
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<222> (371)
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<221> misc feature
<222> (397)
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<220>
<221> misc feature
<222> (409)
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<222> (436)
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<222> (444)
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<221> misc feature
<222> (452)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (466)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (479)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (490)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (519)
<223> n equals a,t,g, or c
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<222> (553)
<223> n equals a,t,g, or c
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<400> 736

PCT/US00/05882

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tegacecaeg egteegeeea egeteeggee teagecetae eageaetggt eatgtetaaa 60
ggtcatcgta ttgaggaagt tcctgaactt cttntggtag ttgaagataa agttgaaggc 120
tacaagaaga ccaaggaagc tgttttgctc cttaagaaac ttaaagcctg ggaatgatat 180
caaaaaggtc tatgcctctc agcgaatgag agctgggcaa aggcaaaatg gagaaaccgt 240
cgccgtatcc agcgcagggc ccgtgcatca tctataatga ggataatggt atcatcaagg 300
ccttccagaa acatccctgg aattactctg cttnaatgtn aagcaagctg aaacattttg 360
naagcttgct ncctggtggg gcatgtgggg acgtttncgg cattgggang gaaatggctt 420
ttccgggant ttaganggan tgtnacgggc antgggcgta aagcgntttc cctccaagng 480
ttaactacan tcttcccagg caccaagatg gattaatana gatcttggca gaatctggaa 540
aagcccagag gtnccaaggg cccttcgggc accagc
<210> 737
<211> 297
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (7)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (243)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (254)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (261)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (266)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (275)
<223> n equals a,t,g, or c
<400> 737
gctccgncat ggcgtgtgct cgcccactga tatcggtgta ctccgaaaag ggggagtcat 60
ctggcaaaaa tgtcactttg cctgctgtat tcaaggctcc tattcgacca gatattgtga 120
actttgttca caccaacttg cgcaaaaaca acagacagcc ctatgctgtc agtgaattag 180
caggicatca gactagiget gagicitigg giactiggeag agetigget egaatteeca 240
```

297

ganttcgagg tggngggact naccgntctg gccanggtgc ttttggaaac atgtgtc

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<210> 738
<211> 354
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (26)
<223> n equals a,t,g, or c
<220>
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<222> (74)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (80)
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<222> (84)
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<222> (98)
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<222> (120)
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<220>
<221> misc feature
<222> (148)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (193)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (286)
<223> n equals a,t,g, or c
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<222> (303)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (329)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (351)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (353)
<223> n equals a,t,g, or c
<400> 738
gcgagaatga agactattct cagcantcag actgtcgaca ttccagaaaa tgtcgacatt 60
actctgaagg gacncacagn tatngtgaag ggccccanag gaaccctgcg gagggacttn 120
aatcacatca atgtataact cagccttntt ggaaagaaaa aaaagaggct ccgggttgac 180
aaatggtggg gtnacagaaa ggaactggct accgttcgga ctatttgtag tcatgtacag 240
aacatgatca agggtgttac actgggcttc cgttacaaga tgaggnctgt gtatgctcac 300
ttncccatca acgttgttat ccaagagant gggtctattg ttgaaatcca nant
<210> 739
<211> 504
<212> DNA
<213> Homo sapiens
<400> 739
cegecateat gggtegeatg catgeteecg ggaagggeet gteecagteg getttaceet 60
ategacgcag egteeceact tggttgaagt tgacatetga egacgtgaag gagcagattt 120
acaaactggc caagaagggc cttactcctt cacagatcgg tgtaatcctg agagattcac 180
atggtgttgc acaagtacgt tttgtgacag gcaataaaat tttaagaatt cttaagtcta 240
agggacttgc tcctgatctt cctgaagatc tctaccattt aattaagaaa gcagttgctg 300
ttcgaaagca tcttgagagg aacagaaagg ataaggatgc taaattccgt ctgattctaa 360
tagagagccg gattcaccgt ttggctcgat attataagac caagcgagtc ctccctccca 420
attggaaata tgaatcatct acagcctctg ccctggtcgc ataaatttgt ctgtgtactc 480
aagcaataaa atgattgttt aact
                                                                   504
<210> 740
<211> 399
<212> DNA
<213> Homo sapiens
<400> 740
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ggaccegeca acatgggeeg egttegeaec aaaacegtga agaaggegge eegggteate 60
atagaaaagt actacacgcg cctgggcaac gacttccaca cgaacaagcg cgtgtgcgag 120
gagategeca ttatececag caaaaagete egeaacaaga tageaggtta egteaegeat 180
ctgatgaagc gaattcagag aggcccagta agaggtatct ccatcaagct gcaggaggag 240
gagagagaaa ggagagacaa ttatgttcct gaggtctcag ccttggatca ggagattatt 300
gaagtagatc ctgacactaa ggaaatgctg aagcttttgg acttcggcag tctgtccaac 360
cttcagtcac tcagcctaca gttgggatga tttcaaaac
<210> 741
<211> 431
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (335)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (393)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (417)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (425)
<223> n equals a,t,g, or c
<400> 741
aaacaacggt cgtgccaaaa agggccgcgg ccatgtgcag cccattcgct gcacgaactg 60
cgcccggtgc gtgcccaagg ataaggccat caagaagttt gtcattcgga acattgtaga 120
agccgctgct gtcagggaca tatctgaagc aagcgtcttc gacgcctacg tgcttcccaa 180
gctctatgtc aagctgcatt attgcgtgac tgtgccatcc atagcaaggt tgttaggaat 240
cgatcccgct aagcccggaa ggaccgaaca cccccaccac gattcagacc tgctggcgct 300
gcaccttcga cctccaccaa agcccatgta aagangccgt ttttgtaagg acggaaggaa 360
aattaccttg gaaaaataaa atggaagttg tanttttaaa aaaaaaaaa aaacccnagg 420
ggggncccgt c
                                                                   431
<210> 742
<211> 357
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (178)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (240)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (273)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (297)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (324)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (352)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (353)
<223> n equals a,t,g, or c
<400> 742
gtgcagcggt tcattaaaat cgatggcaag gtccgaactg atataaccta ccctgctgga 60
ttcatggatg tcatcagcat tgacaagacg ggagagaatt tccgtctgat ctatgacacc 120
aagggtcgct ttgctgtaca tcgtattaca cctgaggagg ccaagtacaa gttgtgcnaa 180
gtgagaaaga totttgtggg cacaaaagga atcoctcato tggtgactca tgatgcccgn 240
accatcogct accccgatcc cctcatcaag gtnaatgatc cattcatatt gatttanaga 300
ctggcaagat tactgatttc atcnatttcg acactggtaa cctgtgtatg gnnactg
<210> 743
<211> 249
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (42)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
  <222> (77)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (115)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (122)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (158)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (200)
  <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (215)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (221)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (248)
 <223> n equals a,t,g, or c
 <400> 743
 ggggcggtat gccgccaaac gcttccgcaa agctcagtgt cncattgtgg agcgcctcac 60
 taactccatg atgatgnacg ggcgcaacaa cggcaagaag ctcatgactg tgcgnatcgt 120
cnagcatgee ttegagatea taegeetget cacaggenaa gaaccetetg caggteetgg 180
 tgaacgccat catcaacatn ggtccccggg aagantccac ncgcattggg cgcgccggga 240
 ctgttgana
                                                                     249
 <210> 744
 <211> 383
 <212> DNA
 <213> Homo sapiens
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<221> misc feature

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<400> 744
 gaagaattgc atcgtgctca tcgacagcac accgtaccga cagtggtacg agtcccacta 60
 tgcgctgccc ctgggccgca agaagggagc caagctgact cctgaggaag aagagatttt 120
aaacaaaaaa cgatctaaaa aaattcagaa gaaatatgat gaaaggaaaa agaatgccaa 180
aatcagcagt ctcctggagg agcagttcca gcagggcaag cttcttgcgt gcatcgcttc 240
aaggccggga cagtgtggcc gagcagatgg ctatgtgcta gagggcaaag agttggagtt 300
ctatcttagg aaaatcaagg cccgcaaagg caaataaatc cttgttttgt cttcacccat 360
gtaataaagg tgtttattgg ttt
<210> 745
<211> 452
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (314)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (328)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (334)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (352)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (403)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (416)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (429)
<223> n equals a,t,g, or c
<220>
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<222> (435)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (451)
<223> n equals a,t,g, or c
<400> 745
gcgcacgatg cctggagtta ctgtaaaaga cgtgaaccag caggagttcg tcagagctct 60
ggcagccttc ctcaaaaagt ccgggaagct gaaagtcccc gaatgggtgg ataccgtcaa 120
gctggccaag cacaaagagc ttgctcccta cgatgagaac tggttctaca cgcgagctgc 180
ttccacageg eggeacetgt aceteegggg tggegetggg gttggeteca tgaccaagat 240
ctatggggga cgtcagagaa acggcgtcat gcccagccac ttcagccgag gctccaagag 300
tgtggcccgc cggntcctcc aagccctngg aggngctgaa aatggtggaa anggaccaag 360
atggcggccc gcaaactgac acctcaggga caaagagatc tgnacagaat cgccgnacag 420
gtggcagent gccancaaag aagcattaga nc
<210> 746
<211> 114
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (22)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (55)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (85)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (98)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (103)
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<223> n equals a,t,g, or c
<400> 746
tgcatgctgg ngctggtcct gnccttgctg tcctccagct ctgctgagga gtacntgggc 60
ctgtctgcaa accaatgtgc cgtgncagcc aaggacangg tgnactgtgg ctac
<210> 747
<211> 165
<212> DNA
<213> Homo sapiens
<400> 747
ggcacageca eccagggeet gagteetgte cacaceccag gtgacggeeg getecacaag 60
gcagtgagcg tgggcccccg ggtgcacatc attgaggagc tgcagatctt ctcatcggga 120
cagecegtgg cagaatetge teetgggaca eccaeagggg ggetg
<210> 748
<211> 583
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (46)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (291)
<223> n equals a,t,g, or c
<220> -
<221> misc feature
<222> (341)
<223> n equals a,t,g, or c
<220>
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<222> (387)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (458)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (462)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (480)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (537)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (541)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (543)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (546)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (580)
<223> n equals a,t,g, or c
<400> 748
ggctagaaga tggttttgga gagcacccct tttaccactg cctggntgca gaagtgccga 60
aagagcactg gactccggaa ggacacagca ttgttggttt tgccatgtac tattttacct 120
atgacccgtg gattggcaag ttattgtatc ttgaggactt cttcgtgatg agtgattata 180
gaggetttgg cataggatca gaaattetga agaatetaag ceaggttgea atgaggtgte 240
aaaagaagag gtgcttctga tctgtccagt gaagaaggtt ngagacttgt taagaatcga 360
caaggagtct tgctaaaaat ggcaacntag gagtgaggaa tgcttgctgt agatgacaac 420
ctccattcta ttttagaata aaattcccca actttctntt gnttttctat gctggttggn 480
agtgaaatta atttaaatga gcacccattt caaaagcttt aattaccaag tgggcgnttg 540
ntnccntgtt ttgaaaattg aaggtcttgt tttaaaaggn ggc
<210> 749
<211> 419
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (3)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (16)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (24)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (29)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (30)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (169)
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<220> ,
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<222> (342)
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<220>
<221> misc feature
<222> (351)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (376)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (398)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (419)
<223> n equals a,t,g, or c
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<400> 749
acnoggaggo ttottnatta oggnogggnn tgatgaggga aagotggtga ogcotgcagg 60
tgaccggtcc ggaattcccg ggtcgaccca cgcgtccggg cgtgatgtct cacagaaagt 120
totocgotoc cagacatggg tocotoggot tootgootog gaagogoana goaggoatog 180
tgggaaggtg aagagcttcc ctaaggatga cccgtccaag ccggtccacc tcacagcctt 240
cctgggatac aaggctggca tgactcacat cgtgcgggaa gtcgacaggc cgggatccaa 300
ggtgaacaag aaggaggtg gtggaggctg tgaccattgt anagacacca nccatggtgg 360
tttgtgggca ttgttngcta cgttggaaaa ccctcgangg ctccggaact tcaagaatn 419
<210> 750
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (453)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (475)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (497)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (499)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (503)
<223> n equals a,t,g, or c
<400> 750
ggccgaacat ggagatcaag attatatctg gcactgcatt gatctcttct tagatttcat 60
tactgtcttc agaaaactca tgatgatcct ggccatgaat gaaaaggata agaagaaaga 120
gaagaaatga agtgaccatc cagcctttcc caattagact tcctctcctt ccacccctca 180
tttccttttt gcacacatta caggtggtgt gttctgtgat aatgaaaagc atcagaaaag 240
cttttgtact ttgtggtttc ctctattttg aattttttga tcaaaaaact gattagcaga 300
atatagtttg gagtttggct tcatcttcct qqqgttcccc tcactccctt ttttqqcaac 360
cccatctgta gcctcttcct ctactcaggc agtcgacccg ccacgatgag aagtgggacc 420
agcagagggc gccaacttca ggagcccgct ttnccaccca gcttcattca cccantggac 480
ctgaactgtt tgggtananc ccnccgg
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<211> 435
 <212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (23)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (31)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (34)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (110)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (134)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (151)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (158)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (199)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (215)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (218)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (226)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (239)
 <223> n equals a,t,g, or c
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<221> misc feature
 <222> (243)
 <223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (257)
<223> n equals a,t,g, or c
`<220>
<221> misc feature
<222> (295)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (321)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (324)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (331)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (355)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (363)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (365)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (403)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (420)
<223> n equals a,t,g, or c
<400> 751
nactggaagt nctccgggag aanggatete nacngcggtg ccggacgete tagaactagt 60
ggatcccccg ggctgcaggt agcctgagct tagctcagcg ccggggcttn accaaqacct 120
acactgttgg ctgngaggaa tgcacagtgg ntccctgntt atccatcccc tgcaaactgc 180
agagtggcac tcattgctng tggacggacc agctnctnca aggctntgaa aagggcttnc 240
agnocceptca cottgentge etgeoteggg agecaggget gggcacetgg cagtneetge 300
ggtcccagat agcctgaata ntgnccggag nggaagctga agcctgcaca gtgtncaccc 360
tgntnccact cccatctttc tttcggacaa tgaaataaag agntaccacc cagcaaaaan 420
aaaaaaaaa acctg
                                                                   435
<210> 752
<211> 591
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (195)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (240)
<223> n equals a,t,g, or c
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<222> (319)
 <223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (345)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (365)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (407)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (452)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (456)
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<220>
<221> misc feature
<222> (480)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (556)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (570)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (572)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c

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<220>
 <221> misc feature
<222> (579)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (586)
<223> n equals a,t,g, or c
<400> 752
gcggcacgag gcgcccagag agacaccaga gaacccacca tggccccctt tgagcccctg 60
gcttctggca tcctgttgtt gctgtggctg atagccccca gcagggcctg cacctgtgtc 120
ccaccccacc cacagacggc cttctgcaat tccgacctcg tcatcagggc caagttcgtg 180
gggacaccag aagtnaacca gaccacctta taccagcgtt atgagatcaa gatgaccaan 240
atgtataaag ggttccaagc cttaggggat gccgctgaca tccggttcgt ctacaccccc 300
gccatggaga gtgtctgcng atactttcac aggtcccaca accgnagcga ggagtttctc 360
attgntggaa aactgcagga tggacttttg cacatcacta cctgcanttt tgtggctccc 420
tggaacagcc tgagcttagc tcagcgccgg gncttnacca agacctacac tgttggctgn 480
gaggaaatgc acaagtgctt ccctgtttat ccatcccctg caaactgcag agtgggcact 540
cattgcttgt aggacngacc agetectacn angetettna aaaggnettt c
<210> 753
<211> 547
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (429)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (454)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (489)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (503)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (512)
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<400> 753
aagcacttgt ccagatgagc agtgtgtgaa ttctcctgga tcttaccagt gcgttccctg 60
cacagaagga ttccgaggct ggaatggaca gtgccttgat gtggacgagt gcctggaacc 120
aaacgtctgc gcaaatggtg attgttccaa ccttgaaggc tcctacatgt gttcatgcca 180
caaaggctat acccggactc cggaccacaa gcactgtaga gatattgatg aatgtcagca 240
agggaatcta tgtgtaaacg ggcagtgcaa aaataccgag ggctccttca ggtgcactgt 300
ggacaggggt taccagctgt cggcagctaa agaccagttt gaagacattg atgaatgcca 360
caccytcatc tetyttyctc atgggcatgc aagaacactg aagetetttt ccatgtyttt 420
tttgaccang gttacagaac atctgggctt gganacactg tgaaaaattt caatgaatgc 480
ttggaagana aaatttttgc canaaaagaa antgctttat actgcagggt cctatgatgt 540
cttgtcc
                                                                   547
<210> 754
<211> 384
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (307)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (374)
<223> n equals a,t,g, or c
<400> 754
gctcggctcc agcgccatgg cgccctccag gaagttcttc gttgggggaa actggaagat 60
gaacgggcgg aagcagagtc tgggggagct catcggcact ctgaacgcgg ccaaggtgcc 120
ggccgacacc gaggtggttt gtgctccccc tactgcctat atcgacttcg cccggcagaa 180
gctagatccc aagattgctg tggctgcgca gaactgctac aaagtgacta atggggcttt 240
tactggggag atcagccctg gcatgatcaa agactgcgga ccacgtgggt ggtcctgggg 300
cactcanaga gaagcatgtc tttggggaat cagatgagct gattgggcag aaagtggccc 360
atgctctggc aganggactc ggat
                                                                   384
<210> 755
<211> 253
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (60)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (217)
<223> n equals a,t,g, or c
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 <222> (240)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (244)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (252)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (253)
 <223> n equals a,t,g, or c
 <400> 755
 tgtagatctt tgaagactct gattctctga gactgaggag agatgtctta ccagcagcan 60
 cagtgcaagc agccctgcca gccacctcct gtgtgcccca cgccaaagtg cccaagagcc 120
 atgtccaccc ccgaagtgcc ctgagcctta cctgcctcct ccttgtccac ctgagcattg 180
 cccacctcca ccttgccagt ataaatgccc tcctgtngca accataccac cctggcagen 240
 gaanttcccc cnn
                                                                    253
. <210> 756
 <211> 183
 <212> DNA
 <213> Homo sapiens
<220>
 <221> misc feature
 <222> (5)
 <223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (48)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (57)
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.<223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (79)
 <223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (83)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (108)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (141)
<223> n equals a,t,g, or c
<220>
<221> misc feature
·<222> (144)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (146)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (148)
<223> n equals a,t,g, or c
<400> 756
ggcanaaana aggtaggaat aaggctagac ctttaacttc cctaaggnat acttttntag 60
ctaccttctg ccctgtgtnt ggnacctaca tccttaatga ttgtcctntt acccattctg 120
gaattttttt tttttaaaa naantnonga aagcattttg aaaaaaaaa aacaaaaaa 180
aag
                                                                   183
<210> 757
<211> 99
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (12)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (26)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (33)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (77)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (79)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (82)
<223> n equals a,t,g, or c
<400> 757
agcetttaat anateatata ggaaantggt agntgeagta eggtnggaat teegggtgae 60
tcagcgtccg ggattgnanc anctgggatt ggagtttgg
<210> 758
<211> 60
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (36)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (38)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (40)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (45)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (46)
<223> n equals a,t,g, or c
<210> 759
<211> 66
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (6)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (59)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (63)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (65)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (66)
<223> n equals a,t,g, or c
ccntnn
                                                      66
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<210> 760
<211> 487
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (409)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (433)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (473)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (475)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (477)
<223> n equals a,t,g, or c
<400> 760
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ccaggcggac aaagttcagt gtcgggaatt ttccccgtga cattcactgg ggcatgagat 120
tttggaagaa gttttttact ttggtttagt ctttttttcc ttccttttta ttcagctaga 180
atttctggtg ggttgatggt agggtataat gtgtctgtgt tgcttcaaat tggtctgaaa 240
ggctatcctg ctgaaagtcc tgctttccta tctagcattt atttctctgg caaacttttc 300
tttcttttct tttttaaagt aaacttgtgt attgagctta actgtatttc agtatttcca 360
gcttatgtgt acattattcc aatgataccc aacagttatt tatattttnt aacaaattca 420
cagtotgaat gangaottta tttoatggat tataataagg aatgaggtaa ttngngnoto 480
acattca
<210> 761
<211> 422
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (253)
<223> n equals a,t,g, or c
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<220>
  <221> misc feature
  <222> (297)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (350)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (353)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (382)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (403)
  <223> n equals a,t,g, or c
  <220>
  <221> misc feature
  <222> (406)
  <223> n equals a,t,g, or c
  <400> 761
  gaaaaggcta aaatcatgaa ttagttacaa gcaacagtac caacttatgt gacccctgag 60
  gggtggggct gtgagctctt aatttgtttt tgattctgaa aaactctgct tcctggcatc 120
  caggagttag agattgagcc tttcatcttc tttctcaaaa ctagtttttg atgctttctt 180
  tcatgggaat agtcactttt ttatttagta aatcgcattg ctggaaccac caaggatgtg 240
  gaatgtcctt gantgtatta tttatgcaag tcacagtcac gtttgccatc atggcantat 300
  ttgaaacact aataatgtgt ttttactttt ttatccccgt taaaatgatn ttnaaaagga 360
  aaaaggtggt tatagcccct anaatttctg ggtccaaatt atnccnaaaa tttcctaaaa 420
  aa
                                                                     422
  <210> 762
  <211> 375
  <212> DNA
/ <213> Homo sapiens
  <220>
  <221> misc feature
  <222> (279)
  <223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (315)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (373)
<223> n equals a,t,g, or c
<400> 762
tttgaccact tgccaagtcc ctgtctcttt cagacacaga caagcttcat ttaaattatt 60
tcaactgatg aagtaacaat aaagttataa atgataatga tcagatgaaa taatttataa 120
ctttattgtt acttcatcag tgtttccttt tgaaaggtgt atgaattcat tacattttta 180
ttctaatgta ttatctgtag attagaagat aaaatcaagc atgtatctgc ctatactttg 240
tgagttcacc tgtctttata ctcaaaagtg tcccttaana gtgtccttcc ctgaaataaa 300
tacctaaggg agtgnaacag tctctggagg accactttga gcctttggaa gttaagggtt 360
cctcagccac ctngt
<210> 763
<211> 372
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (261)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (301)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (320)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (338)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (344)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (354)
<223> n equals a,t,g, or c
<400> 763
caatatgtag cttactcttt ttttcccccc ttcttaaacc accagtggtt catttttaag 60
atttttcat caagagaaga ataactttac taaattttat ttctttattt gcaaaagaat 120
ctttattaaa acaaacaatc ttaactatgc acatgatgtg accagatcat cttgaaaata 180
ttcctcttta gtaggaactc tttgttttta actcttggta tggtcagaat ataatacttc 240
cataattact tataattcct ntccgggtac tgggggctat aaatacaact tttttaaatg 300
naattcatgg ttatcaaccn ggctccaagt accattangg ggtnccctat gggnaattac 360
cttgggaaag tc
                                                                   372
<210> 764
<211> 195
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (46)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (52)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (60)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (67)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (71)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (86)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (94)
<223> n equals a,t,g, or c
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<220>
<221> misc feature
<222> (128)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (146)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (151)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (153)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (183)
<223> n equals a,t,g, or c
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cggacgcgtg ggcggacgcg tggggaaagg taagctctag cttaangtct angatttgtn 60
ctttganatt naggaaggta aggatnggtc agangatgta acttgatgtg agcagtaata 120
aacctgtntt aaatatcata ctgtgnatat ntnattgaaa atttatttca gagcggaaaa 180
acnttagcta aaatc
                                                                    195
<210> 765
<211> 103
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (30)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (76)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (83)
<223> n equals a,t,g, or c
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<220>
 <221> misc feature
 <222> (91)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (94)
 <223> n equals a,t,g, or c
 <400> 765
 attaataatg gataccattc taaacaagtn aatccaagtt aagcccgtta aggagaaaga 60
 aattaaggtt agcggntcat gtncaagctg ngtntgaaag tgg
, <210> 766
 <211> 538
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (285)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (316)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (327)
 <223> n equals a,t,g, or c
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 <221> misc feature
 <222> (379)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (436)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (441)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
<222> (445)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (450)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (474)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (504)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (516)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (520)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (522)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (526)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (534)
<223> n equals a,t,g, or c
<400> 766
cccgcgcggg cgcaggcggc cggaatggcg gggcccggct ggggtccccc gcgcctggac 60
ggcttcatcc tcaccgagcg cctgggcagc ggcacgtacg ccacggtgta caaggcctac 120
gccaagaagg acactcgtga agtggtagcc ataaagtgtg tagccaagaa aagtctgaac 180
aaggcatcgg tggagaacct cctcacggag attgagatcc tcaaggcatt cgacatcccc 240
acattgtgca gctgaaagac tttcagtgtg agctgggggc ggggncgctg ccaaaaggag 300
tggagaagga catctntttc aggccgnctc tctgcctctt aaaacaacag ttgggaacag 360
```

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```
ttgaaccaat taatcttanc ttcaatccat tgggaagttt ttttgccggc caaggggggg 420
gccggaaacc ttggtncttc nggcntttcn aatcccaatt aaaccccggc caanggaatt 480
ttcttggccc cttgaaagaa aaanggtttg ggcccncccn tnggtncctt tccnaatg
<210> 767
<211> 415
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (350)
<223> n equals a,t,g, or c
<400> 767
ctttcccaag ggaaacactc agctttctat agaaaattgc actttttgtc gagtaatcct 60
ctgcagtgat acttctggta gatgtcaccc agtggttttt gttaggtcaa atgttcctgt 120
atagtttttg caaatagagc tgtatactgt ttaaatgtag caggtgaact gaactggggt 180
ttgctcacct gcacagtaaa ggcaaacttc aacagcaaaa ctgcaaaaag gtggtttttg 240
cagtaggaga aaggaggatg tttatttgca gggcgccaag caaggagaat tgggcagctc 300
atgettgaga cccaatetee atgatgaeet acaagetaga gtatttaaan gcagtggtaa 360
atttccagga aagccagaag ttaaaggcca aaattgtaaa tcagtcgaga tcggg
<210> 768
<211> 425
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (351)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (381)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (389)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (422)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (423)
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<223> n equals a,t,g, or c
<400> 768
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gaccoctcag gocaggooot gatocagtto tocagggtot ttotcagggt caggtocatg 120
gggagaccat ggggtgcttg tetgacactg acetegecet getgagtece eccateagae 180
tggaagtttg tctccccgt gtgtgtcctg cactaaatgt ccaaaccctg atacaggatg 300
taatgcagag agggccacag gcacaaccca ggcctgacaa tcccgtatgt nggaagtaga 360
actgacccc aacacccaga ngtcatgtng aaatactcac ggtatacatg gaaaaaaaaa 420
annaa
                                                               425
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<222> (158)

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cacaaaatta ttatcaacct aactaaaaca ntccttttct ctnttttcct ggaattatca 180
tggagttttc taattctctn ttttgggaat ngtagattgt ttttgaaatg ctttnacgat 240
gttaaaatan tttatt
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<211> 316
<212> DNA
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<221> misc feature
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<222> (284)
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<220>
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<222> (291)
<223> n equals a,t,g, or c
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<222> (294)
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ctgtctctgg tggagacaat aaggaggagt tacagatgca gccacagatt gatcatctgc 120
ctttaacgtg aatcggagat gctttgtaat ctactgtncc agctgaagca ctncatgtta 180
```

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cgaggaagaa actacaagtn atgttcaaat ctattttggg tcattttnat gtacctttgg 240
gttcaggcat tatttggggg gttttnnttc caaaggaact naantaaagt natnttgctt 300
attaaaaaaa ggaaaa
                                                                   316
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caaaagcngg agcnccaccg enggegaccg enctanaact agtggatece eeggnetgea 60
ggaattca
                                                                   68
<210> 772
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  <221> misc feature
  <222> (155)
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  <220>
  <221> misc feature
  <222> (189)
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  <222> (225)
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<222> (572)

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<222> (257)
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attatacaca tacaaaatng gtacagagtc ttttncttcc tcccacccct agggggaaaa 180
actgctttnt gctttgggaa gttgtctctg aaacccgggg acagnggacg caggncagac 240
taggagggan ccgggang
                                                              258
<210> 773
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<212> DNA
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<222> (559)
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<221> misc feature
<222> (565)
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<221> misc feature
<222> (570)
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<221> misc feature
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cgctagagaa gcaatttctg acccctcttt ctttctctgg tcactcaatt tcaggacagg 120
agttgctcct tcccaaagag ttttggggta tctttctctc cattctaggt tattcggagc 180
ccccttttta ccgttaagga gatctgagtt aatggcttgc tcaagttccc aggaatcggt 240
tgtggactga ggaactcggc cccgggctct tagtacgccg tcccttgttc aggtatccag 300
ggacggttct cacctctgtc ttttctcctt gcaggtgact cctgcacctg cgccggctcc 360
tgcaaatgca aagagtgcaa atgcacctcc tgcaagaaaa gtaagtggga tcctctcttt 420
cctctacccc ttcctgtcct ccagcctgtc ccctcttcac catcctcagg ggaattaaag 480
caagtctggg gatgccccat tgcgccggga aattggtggc ctcctcagtg atccntatca 540
aggagaagca aggaatcent aattneeggn gneegttgta ettaact
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<211> 89
<212> DNA
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<222> (74)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (76)
<223> n equals a,t,q, or c
<220>
<221> misc feature
<222> (77)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (79)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (83)
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<220>
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<223> n equals a,t,g, or c

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  <223> n equals a,t,g, or c
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  aaaaaaaaa aaanannana aanaantat
  <210> 775
  <211> 113
  <212> DNA
  <213> Homo sapiens
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 <222> (106)
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 gggtcctttt ccctntnttc agagtggggg gcccaaattt gggcgntctg ttt
<210> 776
 <211> 66
 <212> DNA
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<222> (13)
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<222> (49)
<223> n equals a,t,g, or c
<220>
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<222> (65)
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<400> 776
ggcanaggat ttnaaccctc accttcgtgt ttcccccaat gtttaaaang tttggatggt 60
ttgtng
<210> 777
<211> 441
<212> DNA
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<222> (401)
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<221> misc feature
<222> (436)
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ggaaatagtg tgtgcccttt gaattaatgg agtgacaccg tgattcatga caggattcca 180
tttactggct gtatgccagc tgctgacagt ctataagtct taatagagat ggagtagagg 240
agctgaaggt tggcatctgc tcattgatga caactatgtt tacaatatgt tgtggactag 300
ttggggcact gaggcaggag aatcacgtgg agcccacggg ttcaagacca gcctgggaaa 360
catagcaaga ccttgtttct aaaaaaaaaa aaaaaaaaac ncgaggggg gcccggtacc 420
caattcgccc taaagngagt c
                                                                    441
<210> 778
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<222> (478)
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<222> (481)
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<222> (482)
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cgagaagacc ctatggagct ttaatttatt aatgcaaaca gtacctaaca aacccacagg 120
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```
tectaaacta ecaaacetge attaaaaatt teggttgggg egacetegga geagaaceca 180
acctccgage agtacatget aagacttcae cagtcaaage gaactactat actcaattqa 240
tocaataact tgaccaacgg aacaagttac cctagggata acagcgcaat cctattctag 300
agtocatato aacaataggg tttacgacct cgatnttgga tcaggacatc ccgatngtgc 360
ageogetatt aaaggttegt ttgtteaacg attaaagtee taegtgatet gagtteagae 420
cggagtaatc caggtcggtt tctatctact tcaaattcct ccctggaaaa nnagaagngg 480
nng
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ceteccegga geggagegea cetagggtee etetteegte eccecagece agetaceegt 120
teagaceage agentegggg ggeacecook egecagents cotecetook geteagenet 180
gccaggttcc cccagccatg aatctcttcc gattcctggg aaaactctcc caactcctcg 240
ccatcatctt gctactgctc naaatctgga attcccgctc gtgcgccgaa attcaggaaa 300
aaaacagtcc cgtttggtgt ggggntttca atggccnaat ttgaaatcct ttcacaataa 360
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tntttantct aaaaattttt ttaaagggn

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accaaa
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<211> 255
<212> DNA
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<222> (224)
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gtaactgcgg acaagttgct ttnacctgaa tttnatgata catttcatta aggttccagt 120
tataaaatat tingitaaat attiattaan giggactata gantgcaaac inccattinc 180
cngntaaact tgtttttaaa ttatggccnt aggtaaccca tatngtaggg tattaatttc 240
cttggaacca aacca
                                                                    255
<210> 782
<211> 348
<212> DNA
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<222> (182)
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<222> (296)
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<222> (346)
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tgaatccacc cgagnttggc ctcccaagtg gctgggcatt ataggcgtga gcactcacgt 120
concected anathecata tteanagang cantiteagt teetteetan gettigting 180
tnaaggggct ccactgactt cctaggccct gtaaatttaa accagtcttt aaggttttgc 240
caggaaagtt cccttctttc caagtgggtt tttccaaatg ggcacaatgg caagcnanac 300
agaggangaa acattaaaaa aannaaaaaa aatttggggg ggggnncc
<210> 783
<211> 160
<212> DNA
<213> Homo sapiens
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<222> (47)
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<222> (49)
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atctgatgaa aaggtcanac tnaaacgcct tgcacggctt ctcggcttga tcacagctcc 120
ctaggtaggt naccacagag nngncncttc tagtgagcct
                                                                   160
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<212> DNA
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caaaaaaaa aaaaaannng n
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724

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tggnacctcc tggtgcccct ggtccttgct gtggtggtgt tngagccgct gccattgctg 240
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<220>
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<220>
<221> misc feature
<222> (501)
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cacaccaccc cttgccaaan tcatctgcct gctccccggg gggagangac cgccggcctc 120
tnctactage ccaecagece accagggana aaataaneca tganangeng egneegecae 180
congtgtnon canteccone ettecegntt ecettagaan eetgeegegt eetateteat 240
gacgeteatg gaacenettt etttgatetn etntntetta tetececete tttntngtte 300
taaagaaaat cattttgatg caaggtcctg cctgnnatca natccgaagt gctcctgcag 360
tnaccetttn cetggcattt etetteeaeg egacaagtet getagtgaga tettgeatga 420
ctcactttgt ttccaaaacc cggggctatt ttgcatctca agtttcctgg ggcctgcttc 480
ctgtgtncca cttaagggcn nctgggccaa gactgt
                                                            516
<210> 801
<211> 284
<212> DNA
<213> Homo sapiens
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<222> (12)
<223> n equals a,t,g, or c
<220>
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<222> (28)
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naageneeg gngaacttgg ggaaggeneg eetgeaggta eeggteegga atteeegggt 60
atatatatag atatatatag atatatagat atatatagat atatatagat atatagatat 240
atatagatat atagatatat atatatctgg ctcatgcatg aaaa
<210> 802
<211> 153
<212> DNA
<213> Homo sapiens
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<220>

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<222> (134)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (140)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (143)
<223> n equals a,t,g, or c
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cggacggctg tgtagcgcgt gggtgtaaga cttgcccaag tcccanagca cctcacctcc 60
cgaagccacc atccccaccc tgtcttccac anccgcctga aagccacaat gagaatgant 120
cacactgagg cctngatgtn ctntaatcac ttg
<210> 803
<211> 383
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (271)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (301)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (370)
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<222> (374).
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<222> (375)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (383)
<223> n equals a,t,g, or c
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cacgtgagat taaaaccaat tttttcccca ttttttctcc ttttttctct tgctgcccac 60
attgtgcctt tattttatga gccccagttt tctgggctta gtttaaaaaa aaaatcaagt 120
ctaaacattg catttagaaa gcttttgttc ttggataaaa agtcatacac tttaaaaaaa 180
aaaaaaactt tttccaggaa aatatattga aatcatgctg ctgagcctct attttctttc 240
tttggatgtt ttggattcag tattccttta nccataaatt tttagcattt aaaaattcac 300
nggatggtac attaagccaa taaactggct ttaatggatt acccaaaaaa aaaaaaaaa 360
aaagggggn cgcnncagag ggn
                                                                   383
<210> 804
<211> 509
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (94)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (397)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (399)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (401)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (434)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (478)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (501)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (504)
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ctctggagct cagcacagcc ctggagcacc aggngtacat tacttttctt gaagacctca 120
agagttttgt caagagccag tagagcagac agatgctgaa agccatagtt tcatggcagg 180
ctttggccag tgaacaaatc ctactctgaa gctagacatg tgctttgaaa tgattatcat 240
cctaatatca tgggggaaaa aataccagat ttaaattata tgttttgtgc tctcatttat 300
ttatcatttt tttctgtaca aatctattat ttctaggttt ttgtattaca tgatagacat 360
aaattgggtt atctcctcca ggcagtttgt cttttcnant nctccccctt caaccgtgtc 420
acaaagacca gacngtgtcg ggaaagtttt ttttctccgt attgttaaag gttccatnca 480
attaggttta ataaaggctt nttntccag
                                                                   509
<210> 805
<211> 753
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (1)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (648)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (668)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (718)
 <223> n equals a,t,g, or c
<220>
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<222> (736)
<223> n equals a,t,g, or c
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ncaaacccac tccaccttac taccagacaa ccttagccaa accatttacc caaataaagt 60
ataggcgata gaaattgaaa cctggcgcaa tagatatagt accgcaaggg aaagatgaaa 120
aattataacc aagcataata tagcaaggac taacccctat accttctgca taatgaatta 180
actagaaata actttgcaag gagagccaaa gctaagaccc ccgaaaccag acgagctacc 240
taagaacagc taaaagagca cacccgtcta tgtagcaaaa tagtgggaag atttataggt 300
agaggcgaca aacctaccga geetggtgat agetggttgt ccaagataga atettagtte 360
aactttaaat ttgcccacag aaccctctaa atccccttgt aaatttaact gttagtccaa 420
agaggaacag ctctttggac actaggaaaa aaccttgtag agagagtaaa aaatttaaca 480
cccatagtag gcctaaaagc agccaccaat taagaaagcg ttcaagctca acacccacta 540
cctaaaaaat cccaaacata taactgaact cctcacaccc aattggacca atctatcacc 600
ctatagaaga actaatggta gtataagtaa catgaaaaca ttctcctncg cataagcctg 660
cgtcaganta aaacctgact gacaattaac agcccaattc tacaatcaaa caacaagnca 720
ttattaccct tactgncaac ccaaccaggc atg
<210> 806
<211> 404
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (352)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (383)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (396)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (398)
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (403)
<223> n equals a,t,g, or c
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aaactaaagc tgaagaggta ctttccataa atacctccca ctgattgaat cagtgtcttt 120
aaagaaattt ctcaatcctt cagccggtga tagcacgttc ttaatgtctc tttttattgc 180
ctgtaatgtt attgcagatc cacatctctc gctcaactgt taatgtctca acctccagag 240
gcaccccacc cagcacactg tcagtaaagg ggcagaatga aacagtgaga gttaagggta 300
caggaagaaa atttgcatgt ttgcaagtga ctagaatcag atagtaagtg gnggtgggtt 360
tttttttta atcattatga aanagtggga agcttngnag gtna
<210> 807
<211> 428
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (17)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (20)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (33)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (89)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (164)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (198)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (215)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (258)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (266)
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<222> (283)
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<222> (400)
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<221> misc feature
<222> (417)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (423)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (426)
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<400> 807

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aggcagatgc tcctctggtg ggagggtgnt ggcccggcaa gattgaagga tgtgcagggc 120
tteeteteag ageegeecaa aetgeettga tgtgtggagg ggangeaaga tgggtaaggg 180
ctcaggaagt tgctccanga acagtagctg atganctgcc cagagtgcct ggctccagcc 240
tgtacccttg gtatgccntg aacatntggt ttccccaccc aantgcggct aagtctcttt 300
ttccttggat cagccaggcg aaattggggc tttgacaagg aattttctaa ggaaaccttg 360
ttaaccagac aaaacacaac cagggttaca gggggtatgn aagggttttc tgncccngga 420
ggnttnag
<210> 808
<211> 403
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (34)
<223> n equals a,t,g, or c
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<222> (62)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (85)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (257)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (258)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (261)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<222> (265)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (270)
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<221> misc feature
<222> (286)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (288)
<223> n equals a,t,g, or c
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<222> (342)
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<221> misc feature
<222> (346)
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<222> (349)
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<222> (365)
<223> n equals a,t,g, or c
<220>
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<222> (375)
<223> n equals a,t,g, or c
<400> 808
enageceega ggggeteteg ettetggege caangeeegg eegeggeeg geegggeega 60
cneegeteeg gggacagtge caggngggga gtttgaetgg ggcggtacae etgteaaaeg 120
gtaacgcagg tgtcctaagg cgagctcagg gaggacagaa acctcccgtg gagcagaagg 180
gcaaaagctc gcttgatctt cattttcagt acgaatacag accgtgaaag ccgggcctca 240
cgatcctcct gaccttnncg ntttncagcn ggaggtgtca gaaaantnac cacagggata 300
actcgcttgt cgcggccaag cgttcatagc gacgtcgctt tnccangtnc gatgtcggat 360
cttcntatca ttgtnaagca gaattcacca agcgttggat tgt
                                                                   403
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<211> 583
<212> DNA
<213> Homo sapiens
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<222> (376)
<223> n equals a,t,g, or c
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<222> (377)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (421)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (423)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (435)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (440)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (444)
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<220>
<221> misc feature
<222> (472)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (478)
<223> n equals a,t,g, or c
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<213> Homo sapiens

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<220>
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<222> (481)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (488)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (565)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (571)
<223> n equals a,t,g, or c
<220>
<221> misc feature.
<222> (573)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (581)
<223> n equals a,t,g, or c
<220>
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<222> (583)
<223> n equals a,t,g, or c
<400> 809
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tttgaagacc acttggctgt ttcacaaaac cagaagtaat tacagggtgt tcctgaaaag 120
ccccatagtg attgagtctt caaaaccacc gattctgaga gcaaggaaga ttttggaaga 180
aaatctgact gtggattatg acaaagatta tctttttct taagtaatct atttagatcg 240
ggctgactgt acaaatgact cctggaaaaa actcttcacc tagtctagaa taagggaggt 300
gggagaatga tgacttaccc tgaagtcctt cccttgactg cccgcactgg ggcctgttct 360
gtgccctggg agcatnntgc ccagctaagt ggggttcagg cagtgggcag ctttcccaat 420
nantegattt ccatnecagn gganttaaaa ccagttggcc aaatttccaa gnccttgnaa 480
ntaaggantc catttaccaa cccgcggttt tgtggtcagt gccccaaggg ggtaggttga 540
agggggctta acaaacatgg aagtnggggg nanaagggat nan
<210> 810
<211> 272
<212> DNA
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<220>
<221> misc feature
<222> (33)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (43)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (123)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (130)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (163)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (165)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (167)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (228)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (259) -
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (262)
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<220>
<221> misc feature
<222> (265)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (266)
<223> n equals a,t,g, or c
<400> 810
ttttttttt tttttggacg ttaaaggcat ttnattccag cgncttctag agagcttagt 60
gtatacagat gagggtgtcc gctgctgctt tccttcggaa tccagtgctt ccacagagat 120
tancctgtan cttatatttg acattcttca ctgtctgttg ttnancnacc gtagcttttt 180
acceptcact teccetteca actateteca gatetecage etecteenet etegacette 240
tccaaaggca ctgaccctng gnctnnactt tg
<210> 811
<211> 300
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (252)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (259)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (264)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (276)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (280)
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<400> 811

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ggcagagnat aaaatcttaa agcactcata atatggcatc cttcaatttc tgtataaaaag 60
cagatetttt taaaaagata ettetgtaae ttaagaaaee tgggeattta aateatattt 120
tgtctttagg taaaagcttt ggtttgtgtt cgtgttttgt ttgtttcact tgtttccctc 180
ccagccccaa accttttgtt ctctccgtga acttaccttt ccctttttct ttctcttttt 240
tttttttgga anattaatng tttncaataa aatttncatn gccattaaaa aaaaaaaaaa 300
<210> 812
<211> 478
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (232)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (294)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (325)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (336)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (409)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (427)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (445)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (460)
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<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (468)
<223> n equals a,t,g, or c
<400> 812
gccaccttac taccagacaa ccttagccaa accatttacc caaataaagt ataggcgata 60
gaaattgaaa cctggcgcaa tagatatagt accgcaaggg aaagatgaaa aattatagcc 120
aagcataata tagcaaggac taacccctat accttctgca taatgaatta actagaaata 180
actttgcaag gagagccaaa gctaagaccc ccgaaaccag acgagctacc tnagaacagc 240
tgaaagagca cacccgtcta tgtagcaaaa tagtgggaag atttataggt tgangcgaca 300
aacctaccga gcctggtgat agctngttgt tccaanattg aatccttagt tccactttta 360
atttggcccc aaaaaccccc taattcccct tggttaattt taactgttng tcccaaaaaa 420
ggaaccngct ctttgggacc cttanggaaa aaaaccttgn ttaaaaaanaa ttaaaaaa 478
<210> 813
<211> 63
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (49)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (50)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (53)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (57)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (59)
<223> n equals a,t,g, or c
<400> 813
geogegatee tteagactge ceggagageg egetetgeet geogeetgnn tgnetgnene 60
tga
```

<221> misc feature

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<210> 814
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gagggtcctg ctg
<210> 815
<211> 102
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teteetttge etggeeggga gggeettgge ngneeetean en
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aggegggeat aacacagcaa gacgagaaga eectatggag etttaattta ttaatgcaaa 120
cagtacctaa caaacccaca ggtcctaaac taccaaacct gcattaaaaa tttcggttgg 180
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ggcgacctcg gagcagaacc caacctccga gcagtacatg ctaagacttc accagtcaaa 240
gcgaactact atactcaatt gatccaataa cttgaccaac ggaacaagtt accctaggga 300
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ggatcaggac attccaatg
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<221> misc feature

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 ctcccccagc cccgccaaga agcgacangg ccccaagncc cgagccggcc gtcaagggga 180
 ccggngtggc tngggttgct naagaaagcg gaatncgggg ggcatcccag ccaagaangn 240
 cccggctggg naggagaanc tngggaacgc cggcctcctt ggncgctgaa ttnccgaaca 300
 ttttggaacc ggattccaga ggaacaaagg gcccgnggnc cttgnttaan aatncggggg 360
 congnaaang tincocotty gggnttitty gaanaanaac ctgggaaaga aagcanotta 420
 agggggggn attttcgggg gaaancgtta tttttaatca aagctaaatt ggggattttn 480
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<223> n equals a,t,g, or c

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<222> (256)
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<223> n equals a,t,g, or c
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ctcactaatg ggaacanaag ctggagctcc accgngtagg cggncggtct agaactagtg 120
tgatcccccg ggctgcagga attcggcncg agaggaaana gaaaccgtct gaactatgct 180
gnnngccatc atnotnggcc tcatcgcnnt tccatcccta cgcatgcttt acatagcana 240
cgaggtgacg atgccnccct taccatcaag atcanttgnc caccaatggt acttgaacct 300
                                                                   329
acgagtacac ccgaccaccn ggtggacta
<210> 819
<211> 648
<212> DNA
<213> Homo sapiens
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<221> misc feature
<222> (369)
<223> n equals a,t,g, or c
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<222> (518)
<223> n equals a,t,g, or c
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<222> (544)
<223> n equals a,t,g, or c
<220>
<221> misc feature
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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c
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gccactccac cttactacca gacaacctta gccaaaccat ttacccaaat aaagtatagg 60
cgatagaaat tgaaacctgg cgcaatagat atagtaccgc aagggaaaga tgaaaaatta 120
taaccaagca taatatagca aggactaacc cctatacctt ctgcataatg aattaactag 180
aaataacttt gcaaggagag ccaaagctaa aacccccaat aaaccttgaa cagtgaanaa 240
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaacctcgag gtcnacggta tcnataacct 300
tgatatenaa tteggeaena geaaceetea tteeceaace caegeeggag getgegeetg 360
caggacetgn etgacegatt ggtggatect etgaanatga acaegactea ecaetgetea 420
ncgaggentg cttgageaaa atccgccaat tataaaaaaa aaacnetee
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<210> 821
<211> 432
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<220>
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<222> (385)
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<220>
<221> misc feature
<222> (425)
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ttgcacgctc tttaagagtc tgcactggag gaactctgcc attaccagct cccttgttgc 120
agaaggaagg ggaaacatac atttattcat gccagtctgt tgcatgcagg ctttttggct 180
tectacettg caacaaaata attgcaccaa eteettagtg eegatteege ecacagagag 240
tcctggagcc acagtctttt ttgctttgca ttgtaaggag agggactaaa gtgctagaga 300
ctatgtcgct ttcctgagct aacgagagcg ctcgtgaact ggantcaact gctttcaggg 360
aaaaagaaaa aaaaaaaaa aaaanccggg ggggggcccg gtaacccatt tccccctana 420
                                                                   432
gnggnggggt tt
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<222> (367)
<223> n equals a,t,g, or c
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<222> (382)
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<222> (427)
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tcattagtga aagtggtctt ttatgtcctc ccagcagaca gacatcaagg atgagttaac 120
caggagacta ctcctgtgga ctgtggagct ctggaaggct tggtgggagt gaatttgccc 180
acaccttaca attgtggcag gatccagaag agcctgtctt tttatatcca ttccttggat 240
gtcattgggc ctctcccacc gatttcatta cggtgccacg catccatggg atctggggta 300
gtccggaaaa acaaaaggag ggnagacagc ctggtaatgg ataagatcct taccacagtt 360
ttcccanggg gaatacetta tnaancette aactttttt tttcccttaa gaattaaaac 420
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<221> misc feature
<222> (54)
<223> n equals a,t,g, or c
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<222> (71)
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<213> Homo sapiens

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agntgaccca ntctccgncc ctccctgtct gcagctggta
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<222> (165)
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gcccccatcc cgggaggana tgaccaagaa acagtcagct gaactgcctg nttctanagg 120
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<210> 825
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<212> DNA
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tataggcgat agaaattgaa acctggcgca atagatatag taccgcaagg ggaaagatga 120
aaaattataa ccaagcataa tatagcaagg actaacccct ataccttctg cataatgaat 180
taactagaaa taactttgca aggagagcca aagctaagac ccccgaaacc agaacgagct 240
accttagaac agcttaaaga gcacaccct ctatttttgc canaatagtg ggaaagattt 300
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<210> 826
<211> 492
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (337)
<223> n equals a,t,g, or c
<220>
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<221> misc feature
<222> (471)
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<222> (475)
<223> n equals a,t,g, or c
<220>
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ataggcgata gaaattgaaa cctggcgcaa tagatatagt accgcaaggg aaagatgaaa 120
aattataacc aagcataata tagcaaggac taacccctat accttctgca taatgaatta 180
actagaaata actttgcaag gagagccaaa gctaagaccc ccgaaaccag acgagctacc 240
taagaacago taaaagagoa caccogtota tgtagoaaaa tagtgggaag atttataggt 300
agaggcgaca aacctaccga gcctggtgat agctggntgt ccaagataga atcttagttc 360
aactttaaat ttgcccacag aaccctctaa atccccttgt aaatttaact gttagnccaa 420
agaggaacaa gctctttgga cactangaaa aaaccttgta tagagaggaa naaanatttn 480
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<211> 290
<212> DNA
<213> Homo sapiens
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<222> (264)
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aacgggaccg tccttctcgc tccgccccgc gggggtcccc tcgtctctcc tctccccgcc 120
cgccggcggt gcgtgtggga aggcgtgggg tgcggacccc ggcccgacct cgccgtcccg 180
cccgccgcct tctgcgtcgc gggtgcgggc cggcggggtc ctctgacgcn gcagacagcc 240
ctcgctgtcn cctccagtgg angncgactt gcgggcggta ctcctacgan
<210> 828
<211> 420
<212> DNA
<213> Homo sapiens
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<222> (149)
<223> n equals a,t,g, or c
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<222> (334)
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<222> (403)
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<221> misc feature
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<222> (405)
<223> n equals a,t,g, or c
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agcgtgcacc aagggcttgg tctgcggggg ccttggagct cctgctcttc tcccgcacct 120
ccatggatgc actgctgccg agcagageng cctctgccag gccccgccct gggattccta 180
gagactagct tcagttttgc tattttttt aagtgggaga agggtgggca gttatcactg 240
gggaagagag gaccggccac ctgtccagca tgggctccag agccttcctc tctcacaggg 300
cagagtettg teggeaagge ageeteetgg ceantitete tgeteatgtt tetggttage 360
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<210> 829
<211> 298
<212> DNA
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<222> (19)
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<222> (20)
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<222> (269)
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<222> (281)
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<222> (287)
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tggagagtga caaaatggtg acaggtagct ggggacctag gctatctcnc catgaaggtt 120
gttcngctna ttgtatatct gtgtatgtag tgtaactata ttgtacaatg ngaagactgt 180
naactactat ntagggttgt tgcagattga aatttagttg tctcattggc tgtctgagga 240
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<223> n equals a,t,g, or c

agtgtggact tctatatata gatctannnt gaaaactgct ncatgantga aaaccaca

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<210> 830
<211> 516
<212> DNA
<213> Homo sapiens
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<223> n equals a,t,g, or c
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<222> (5)
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cgggggcatc cccttgtccc caagagaccc gacgcttgct tcatggccta cacgttcgag 120
agagagtett egggagagga ggaggagtag ggeegeeteg gggetgggea teeggeeeet 180
ggggccaccc cttgtcagcc gggtgggtag gaaccgtaga ctcgctcatc tcgcctgggt 240
ttgtccgcat gttgtaatcg tgcaaataaa cgctcactcc gaattagcgg tgtatttctt 300
gaagtttaat attgtgtttg tgatactgaa gtatttgctt taattctaaa taaaaattta 360
tattttactt ttttattgct ggtttaagat gattcagatt atccttgnac tttgaggaga 420
agtttcttat ttggagcttt tggaaacagc ttaagctttt aacttggaaa gatangnatt 480
aatccccttc attggtntcc aaaagccaat aangng
<210> 831
<211> 636
<212> DNA
<213> Homo sapiens
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<222> (453)
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<221> misc feature
<222> (530)
<223> n equals a,t,g, or c
·<220>
<221> misc feature
<222> (617)
<223> n equals a,t,g, or c
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caatgttett ggcccatcat gacattgggt agcattaact gtaagttttg tgcttccaaa 120
tcactttttg gtttttaaga atttcttgat actcttatag cctgccttca attttgatcc 180
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tttattcttt ctatttgtca ggtgcacaag attaccttcc tgttttagcc ttctgtcttg 240
 tcaccaacca ttcttacttg gtggccatgt acttggaaaa aggccgcatg atctttctgg 300
 ctccactcag tgtctaaggc accetgette etttgettge atcccacaga etattteeet 360
 catcctattt actgcagcaa atctctcctt agttgatgag actgtgttta tctnccttta 420
 aaaccctacc tatcctgaat ggtctgtcat tgnctgcctt taaaatcctt cctctttctt 480
 cctcctctat tctctaaata atgatggggc ttaagttata cccaaagctn actttacaaa 540
 atatttcctc aagactttgc agaaacacca acaaaatgcc atttaaaaaa ggggattttc 600
 tttaaaggaa ctctaanaca ggcaaggttc tgatgt
                                                                    636
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 <211> 466
 <212> DNA
 <213> Homo sapiens
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 <222> (421)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (443)
 <223> n equals a,t,g, or c
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 <221> misc feature
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 <222> (453)
 <223> n equals a,t,g, or c
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 <221> misc feature
 <222> (466)
 <223> n equals a,t,g, or c
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 agttccctcc ttcttacaga agtattttaa ttcaccccac actagaaatg cagcatcttt 120
 gtggacgtct ttttcacaag cctccaaggc tccttagatt gggtcgttac taaaagtaca 180
 ttaaaacact cttgtttatc gaagtatatt gatgtattct aaagctagta aacttcccta 240
 acgtttaatt gccctacaga tgcttctctt gctgtgggtt ttcttttgtt agtggtctga 300
 aataattatt ttcctgttct attaatacat aagtgtattt tgcacaaaaa aattaacctg 360
 qtcaaataqt qattaccaaa atatatta ataatcttgg gcaaattttt gccatttata 420
 ngaaaacatt tttaacccac ggntangttc tanatttatt ctttcn
                                                                    466
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<210> 833 <211> 405

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 <213> Homo sapiens
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 <221> misc feature
 <222> (278)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (335)
 <223> n equals a,t,g, or c
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 gggaggagtc tgtgcagttt ctgacacttg ttgttgaaca tggctaaata caatgggtat 120
cgctgagact aagttgtaaa aaattaacaa atgtgctgct tggttaaaat ggctacactc 180
 atotgactca ttotttatto tattttagtt ggtttgtato ttgcctaagg tgcgtantcc 240
 aactettggt attaccetce taatagteat actagtante atactecetg gtgttatgta 300
 ttctctaaaa gctttaaatg tctgcattgc aaccngccat caaatattga atgggctctc 360
 ttttggctgg aattacaaac tcaaaaaatg tttctcagga aaaaa
 <210> 834
<211> 402
 <212> DNA
 <213> Homo sapiens
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 <221> misc feature
 <222> (277)
 <223> n equals a,t,g, or c
 <220>
 <221> misc feature
 <222> (332)
 <223> n equals a,t,g, or c
<220>
<221> misc feature
 <222> (354)
 <223> n equals a,t,g, or c
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<221> misc feature
<222> (359)
<223> n equals a,t,g, or c
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<221> misc feature
<222> (390)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (400)
<223> n equals a,t,g, or c
<400> 834
gcaaacccac aggtcctaaa ctaccaaacc tgcattaaaa atttcggttg gggcgacctc 60
ggagcagaac ccaacctccg agcagtacat gctaagactt caccagtcaa agcgaactac 120
tatactcaat tgatccaata acttgaccaa cggaacaagt taccctaggg ataacagcgc 180
aatcctattc tagagtccat atcaacaata gggtttacga cctcgatgtt ggatcaggac 240
atcccgatgg tgcagccgct attaaaggtt cgtttgntca acgattaaag tcctacgtga 300
tctgagttca gaccggagta atccaggtcg gnttctatct acttcaaatt cctncctgna 360
cgaaaggaca agagaaataa gggctacttn acaaagcgcn tt
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<220>
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<221> misc feature
<222> (110)
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<221> misc feature
<222> (117)
<223> n equals a,t,g, or c
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aaaaagggeg geegttntaa aggateeaag ettaegtaen egtgeatgen aegteanage 120
t
<210> 836
<211> 411
<212> DNA
<213> Homo sapiens
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<222> (340)
<223> n equals a,t,g, or c
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<223> n equals a,t,g, or c
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<221> misc feature
<222> (408)
<223> n equals a,t,g, or c
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acttgtggtt gggtcagtgc cgcgcgccgc tcggtcgtta ccgcgaggcg ctggtggcct 120
tcaggctgga cggcgcgggt cagccctggt ttgccggctt ctgggtcttt gaacagccgc 180
gatgtcgatc ttcaccccca ccaaccagat ccgcctaacc aatgtggccg tggtacggat 240
gaagegegee aggaageget tegaaatege ttgetacaga aacaagtegt eggetggegg 300
agggetttgg aaaaagaett gatgaatttt geagaeeean eaangtttgt aaagttneea 360
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aagtcagttt ccaaaaggaa attcancagg ggtttggaaa atgccaanga a
                                                                     411
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 <212> DNA
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 <223> n equals a,t,g, or c
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 ctggccaaga ccacccagga aaccatcgac aagactgcta accaggcctc tgacaccttc 120
 tctgggatcg ggaaaaaatt cggcctcctg aaatgacagc agggagactt gggtcggcct 180
 cctgaaatga tagcagggag acttgggtga cccccttcc aggcgccatc tagcacagcc 240
 tggccctgat ctccgggcag ccaccacctc ctcggtctgc cccctcatta aaattcacgt 300
 тсссаавава вазававава вазававава вазававава вазававава вазававава 360
 aaaaaaaaa aaaaaaaaa ngnnnn
                                                                    386
 <210> 838
 <211> 124
 <212> DNA
. <213> Homo sapiens
 <400> 838
 gettteaata gategeageg agggagetge tetgetaegt acgaaacece gacecagaag 60
 caggtcqtct acgaatggtt tagcgccagg ttccccacga acgtgcggtg cgtgacgggc 120
 gagg
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<211> 270
<212> DNA
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<223> n equals a,t,g, or c
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<222> (56)
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<222> (107)
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<400> 839

<223> n equals a,t,g, or c

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gtgatgtcct gcgccgttct gccccctctc ccttccaggg tgagggnctg gggtgagggt 120
taatgttcgn accagtgctg gctgttcccc tcaccctaac cctctcccca aaggncgnag 180
gggcccggtt acccaattcg ccctatagtg agtcgtatta caattcactg gccgtcgttt 240
tacaagacgn agggaggagn ntgatgaaaa
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<212> DNA
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<222> (262)
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cccataccca accccctggt caacctcaac ctaggcctcc tatttattct agccacctct 120
agcctagccg tttactcaat cctctgatca gggtgagcat caaactcaaa ctacgccctg 180
ateggegeac tgegageagt ageceaaacn ateteatatg aagteacect agecateatt 240
cctactatca acattactaa tnngttggct cctttaacct ctccaccctt atcacaacac 300
aagaacacte etgaatatee tgecateata accetttgge catatatnat tatettecae 360
actagggana acaacgaacc cccttcgaan cttgngaaag ggaatttcna ataatcttca 420
ggttcaaatt
                                                                   430
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<211> 650
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<222> (589)
<223> n equals a,t,g, or c
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<222> (634)
<223> n equals a,t,g, or c
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ttttttacct gagtaggcct agaaataaac atgctagctt ttattccagt tctaaccaaa 120
aaaataaacc ctcgttccac agaagctgcc atcaagtatt tcctcacgca agcaaccgca 180
tccataatcc ttctaatagc tatcctcttc aacaatatac tctccggaca atgaaccata 240
accaataata ccaatcaata ctcatcatta ataatcataa tggctatagc aataaaacta 300
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ggaatagece cettteaett etgagteeca gaggttaeee aaggeaeeee tetgaeatee 360
ggcctgcttc ttctcacatg acaaaaacta gcccccatct caatcatata ccaaatctct 420
ccctcactag acgtaagcct tctcctcact ctctcaatct tatccatcat agtaggcagt 480
tgagggtgga ttaaaccaaa acccagctac gcaaaatcnt agcatacttc ctcaattacc 540
cacataggat gaatnaatag cagnttctac cgnacaaccc ttacataanc atttcttaaa 600
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ccacacttac cttgccaatg gccagaccaa ggtgctgact cagaagttgt catcagtcag 240
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gaagatcagg cettetatee tgggetgeaa cateettega gttgaatatt cettaetgat 360
ctatgttagc gttcctggat ccaagaaggt catccttgac ctgcccctgg taattggcag 420
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gntgggtaga tctgaacatc ctgataccc
<210> 843
<211> 158
<212> PRT
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<213> Homo sapiens

<400> 843

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Gly Pro Phe Pro Lys Asn Leu Val Gln Ile Lys Ser Asn Lys Asp Lys 20 25 30

Glu Gly Lys Val Phe Tyr Ser Ile Thr Gly Gln Gly Ala Asp Thr Pro 35 40 45

Pro Val Gly Val Phe Ile Ile Glu Arg Glu Thr Gly Trp Leu Lys Val 50 60

Thr Glu Pro Leu Asp Arg Glu Arg Ile Ala Thr Tyr Thr Leu Phe Ser 65 70 75 80

His Ala Val Ser Ser Asn Gly Asn Ala Val Glu Asp Pro Met Glu Ile
85 90 95

Leu Ile Thr Val Thr Asp Gln Asn Asp Asn Lys Pro Glu Phe Thr Gln 100 105 110

Glu Val Phe Lys Gly Ser Val Met Glu Gly Ala Leu Pro Gly Thr Ser 115 120 125

Val Met Glu Val Thr Ala Thr Asp Ala Asp Asp Gly Cys Gly Thr Pro 130 135 140

Thr Met Pro Pro Ser Leu Thr Pro Ser Ser Ala Gln Asp Pro 145 150 155

<210> 844

<211> 601

<212> PRT

<213> Homo sapiens

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 Arg Arg Trp Xaa Ser Trp Arg Lys Asp Arg Ala Arg Thr Arg Arg Gln
                              40
 Glu Glu Leu Ala Leu Ser Gln Glu Pro Lys Ser Ser Ser Arg Gly Xaa
 Ser Pro Gly Ala Ser Pro Ala Ser Pro Thr Ser Gln Gln Phe Cys Cys
 65
 Phe Arg Leu Asp Gln Val Ile His Ser Asn Pro Ala Gly Ile Gln Gln
Ala Leu Ala Gln Leu Ser Xaa Arg Gln Xaa Ser Val Thr Ala Pro Gly
                                 105
Gly His Pro Arg His Lys Pro Gly Pro Pro Gln Ala Pro Gln Gly Pro
        115
                             120
Ser Pro Arg Pro Pro Thr Arg Tyr Glu Pro Gln Arg Val Asn Ser Gly
                         135
                                             140
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Leu 145		Ser	Asp	Pro	His 150	Phe	Xaa	Glu	Pro	Gly 155	Pro	Met	Val	Arg	Gly 160
Val	Gly	Gly	Thr	Pro 165	Arg	Asp	Ser	Ala	Gly 170	Val	Ser	Pro	Phe	Pro 175	Pro
Lys	Arg	Arg	Glu 180	Arg	Pro	Pro	Arg	Lys 185	Pro	Glu	Leu	Leu	Gln 190	Glu	Glu
Ser	Leu	Pro 195	Pro	Pro	His	Ser	Ser 200	Gly	Phe	Leu	Gly	Ser 205	Lys	Pro	Glu
	210		Pro			215					220				
Thr 225	Pro	His	Ile	Trp	Asn 230	Arg	Leu	His	Thr	Ala 235	Thr	Ser	Arg	Lys	Ser 240
Tyr	Arg	Pro	Ser	Ser 245	Met	Glu	Pro	Trp	Met 250	Glu	Pro	Leu	Ser	Pro 255	Phe
	-		Ala 260					265					270		_
Leu	Ser	Gly 275	Asp	Ser	Gln	Val	Ser 280	Ser	Gly	Pro	Cys	Ser 285	Gln	Arg	Ser
Ser	Pro 290	Asp	Gly	Gly	Leu	Lys 295	Gly	Ala	Ala	Glu	Gly 300	Pro	Pro	Lys	Arg
Pro 305	Gly	Gly	Ser	Ser	Pro 310	Leu	Asn	Ala	Val	Pro 315	Cys	Glu	Gly	Pro	Pro 320
			Pro	325					330				_	335	_
Arg	Lys	Glu	Leu 340	Pro	Arg	Glu	Gln	Pro 345	Leu	Pro	Pro	Gly	Pro 350	Ile	Gly
Thr	Glu	Arg 355	Ser	Gln	Xaa	Thr	Asp 360	Arg	Gly	Thr	Glu	Pro 365	Gly	Pro	Ile
Arg	Pro 370	Ser	His	Arg	Pro	Gly 375	Pro	Pro	Val	Gln	Phe 380	Gly	Thr	Xaa	Asp
Lys 385	Asp	Ser	Asp	Leu	Arg 390	Leu	Val	Val	Gly	Asp 395	Ser	Leu	Lys	Ala	Glu 400
Lys	Glu	Leu	Thr	Ala 405	Ser	Val	Thr	Glu	Ala 410	Ile	Pro	Val	Ser	Arg 415	Asp

Trp	Glu	Leu	Leu 420	Pro	Ser	Ala	Ala	Ala 425	Ser	Ala	Glu	Pro	Gln 430	Ser	Lys
Asn	Leu	Asp 435	Ser	Gly	His	Cys	Val 440	Pro	Glu	Pro	Ser	Ser 445	Ser	Gly	Gln
Arg	Leu 450	Tyr	Pro	Glu	Val	Phe 455	Tyr	Gly	Ser	Ala	Gly 460	Pro	Ser	Ser	Ser
Gln 465	Ile	Ser	Gly	Gly	Ala 470	Met	Asp	Ser	Gln	Leu 475	His	Pro	Asn	Ser	Gly 480
Gly	Phe	Arg	Pro	Gly 485	Thr	Pro	Ser	Leu	His 490	Pro	туг	Arg	Ser	Gln 495	Pro
Leu	Tyr	Leu	Pro 500	Pro	Gly	Pro	Ala	Pro 505	Pro	Ser	Ala	Leu	Leu 510	Ser	Gly
Val	Ala	Leu 515	Lys	Gly	Gln	Phe	Leu 520	Asp	Phe	Ser	Thr	Met 525	Gln	Ala	Thr
Glu	Leu 530	Gly	Lys	Leu	Pro	Ala 535	Gly	Gly	Val	Leu	Tyr 540	Pro	Pro	Pro	Ser
Phe 545		Tyr	Ser	Pro	Ala 550	Phe	Cys	Pro	Ser	Pro 555	Leu	Pro	Asp	Thr	Ser 560
Leu	Leu	Gln	Val	Arg 565	Gln	Asp	Leu	Pro	Ser 570	Pro	Ser	Asp	Phe	Tyr 575	Ser
Thr	Pro	Leu	Gln 580	Pro	Gly	Gly	Gln	Ser 585	Gly	Phe	Leu	Pro	Ser 590	Gly	Ala
Pro	Ala	Ser 595	Arg	Cys	Phe	Tyr	Pro 600	Trp							

<210> 845

<211> 67

<212> PRT

<213> Homo sapiens

<400> 845

Thr Gln Lys Thr Ser Ser Leu Leu Pro Ala Leu Ser Leu Gln Leu Pro
1 5 10 15

Leu Leu Thr Arg Phe Ser Ile Met Cys Ser Val Lys Glu Glu Phe Trp 20 25 30

WO 00/55350 PCT/US00/05882

791

Arg Val Gln Ser Ile Ile Thr Glu Leu Val Leu Lys Gly Glu Phe Gly
35 40 45

Val Glu Glu Ala Met Lys Leu Ile Thr Gly Thr Glu Ala Lys Tyr Lys 50 55 60

Ser Ile Asp 65

<210> 846

<211> 146

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (16)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 846

Ser Gln Gly Pro Asp His Pro Ser Ser Gln Leu Gln Pro Leu Asn Xaa 1 5 10 15

Ser Leu Ser His Leu Leu Val Pro Cys Leu Ser Ile Met Ser Leu Leu 20 25 30

Asn Lys Pro Lys Ser Glu Met Thr Pro Glu Glu Leu Gln Lys Arg Glu 35 40 45

Glu Glu Glu Phe Asn Thr Gly Pro Leu Ser Val Leu Thr Gln Ser Val
50 55 60

Lys Asn Asn Thr Gln Val Leu Ile Asn Cys Arg Asn Asn Lys Lys Leu 65 70 75 80

Leu Gly Arg Val Lys Ala Phe Asp Arg His Cys Asn Met Val Leu Glu 85 90 95

Asn Val Lys Glu Met Trp Thr Glu Val Pro Lys Ser Gly Lys Gly Lys 100 105 110

Lys Lys Ser Lys Pro Val Asn Lys Asp Arg Tyr Ile Ser Lys Met Phe 115 120 125

Leu Arg Gly Asp Ser Val Ile Val Val Leu Arg Asn Pro Leu Ile Ala 130 135 140

Gly Lys

	0> 8														
	1> 1														
	2> P														
<21	3> н	omo	sapi	ens											
<22	0>														
<22	1> s	ITE													
<22	2> (8) '													
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<22															
<22	1> 5	ITE													
	•	179)													
<22	3> X	aa e	qual	s an	y of	the	nat	ural	ly o	ccur	ring	L,-a	mino	aci	ds
•)> 8														
Ala 1	Arg	Met	Ala	Ala 5	Asp	Lys	Xaa	Pro	Ala 10	Ala	Gly	Pro	Arg	Ser 15	Arq
Ala	Ala	Met	Ala 20	Gln	Trp	Arg	Lys	Lys 25	Lys	Gly	Leu	Arg	Lys 30	Arg	Arg
Gly	Ala	Ala 35	Ser	Gln	Ala	Arg	Gly 40	Ser	Asn	Ser	Glu	Asp 45	Gly	Glu	Phe
Glu	Ile 50	Gln	Ala	Glu	Asp	Asp 55	Ala	Arg	Ala	Arg	Lys 60	Leu	Gly	Pro	Gly
Arg 65	Pro	Leu	Pro	Thr	Phe 70	Pro	Thr	Ser	Glu	Cys 75	Thr	Ser	Asp	Val	Glu 80
Pro	Asp	Thr	Arg	Glu 85	Met	Val	Arg	Ala	Gln 90	Asn	Lys	Lys	Lys	Lys 95	Lys
Ser	Gly	Gly	Phe 100	Gln	Ser	Met	Gly	Leu 105	Ser	Tyr	Pro	Val	Phe 110	Lys	Gly
Ile	Met	Lys 115	Lys	Gly	Tyr	Lys	Val 120	Pro	Thr	Pro	Ile	Gln 125	Arg	Lys	Thr
Ile	Pro 130	Val	Ile	Leu	Asp	Gly 135	Lys	Asp	Val	Val	Ala 140	Met	Ala	Arg	Thr
Gly 145	Ser	Gly	Lys	Thr	Ala 150	Cys	Phe	Leu	Leu	Pro 155	Met	Phe	Glu	Arg	Leu 160
Lys	Thr	His	Ser	Ala 165	Gln	Thr	Gly		Arg	Ala	Ser	Ser	Ser	Arg	Arg

Pro Glu Xaa Trp Pro Cys Arg Pro 180

<21	0> 8	48													
<21	1> 1	60													
<21	2> P	RT													
<21	3> н	ото	sapi	ens											
<22	0>														
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	2> (•													
<22	3> X	aa e	qual	s an	y of	the	nat	ural	ly o	ccur	ring	L-a	mino	aci	ds
	0> 8									_ •	_	_	_		_
	Arg	Ala	Ser		Glu	Cys	Ala	Arg	_	Ala	Ala	Ala	Val	_	Thr
1				5					10					15	
a	•	•	•	•••	•	•• : -	•• • -		a1		•	•	•••		~3
cys	Arg	Arg	Arg 20	HIS	Arg	MIS	HIS		GIN	Leu	Arg	Arg	His	ren	GIU
			20					25					30		
Agn	λla	Yaa	Sor	Glu	Agn	Dha	Aen	Glu	T.Au	T.011	T.170	Δ1 a	Leu	Glu	Val
nsp	niu	35	Jer	GIU	Non	File	40	GIU	Deu	nea	пуз	45	rea	GLY	Vai
		33					40					43			
Asn	Ala	Met	Leu	Arg	Lvs	Val	Ala	Val	Ala	Ala	Ala	Ser	Lys	Pro	His
	50			5	-,-	55					60		-1-	•••	
						-									
Val	Glu	Ile	Arg	Gln	Asp	Gly	Asp	Gln	Phe	Tyr	Ile	Lys	Thr	Ser	Thr
65					70	-	_			75		•			80
Thr	Val	Arg	Thr	Thr	Glu	Ile	Asn	Phe	Lys	Val	Gly	Glu	Gly	Phe	Glu
				85					90					95	
							•								
Glu	Glu	Thr	Val	Asp	Gly	Arg	Lys	Cys	Arg	Ser	Leu	Ala	Thr	Trp	Glu
			100					105					110		
Asn	Glu		Lys	Ile	His	Cys		Gln	Thr	Leu	Leu		Gly	Asp	Gly
		115					120					125			
_	_										_		_		
Pro		Thr	Tyr	Trp	Thr	_	Glu	Leu	Ala	Asn		Glu	Leu	Ile	Leu
	130					135					140				
mb	Dh-	C1	n 7 a	200	7	11-1	17-7	C	mb-	N	T1-	m	17-3	n	~1··
145	rne	GTÅ	WIG	Asp	150	val	AGT	cys	THE	155	TTE	TAL	Val	wrd	160
7.4.3					100					100					100

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<210> 849
<211> 75
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (50)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 849
Val Gln Asn Val Gly Tyr Gln Ser Lys His Cys Gly Ala Val Xaa Tyr
Ala Arg Leu Pro Cys Glu Met Ile Gln Asp Gln Asn Lys Ala Leu Asp
Cys Ser Lys Thr Gln Asn Ser Ser Arg Ala Glu Gly Gly Arg Leu Ile
                             40
Trp Xaa Glu Gly Pro Lys Tyr Lys Thr Asp Gly Leu Arg Leu Glu Thr
                         55
Arg Gly Leu Arg Trp Lys Ala His Val Pro Arg
                    70
<210> 850
<211> 383
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (299)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 850
Ser Thr His Ala Ser Ala His Ala Ser Val Ala Asn Glu Val Ile Lys
                                     10
Cys Lys Ala Ala Val Ala Trp Glu Ala Gly Lys Pro Leu Ser Ile Glu
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Glu	Ile	Glu 35	Val	Ala	Pro	Pro	Lys 40	Ala	His	Glu	Val	Arg 45	Ile	Lys	Ile
Ile	Ala 50	Thr	Ala	Val	Cys	His 55	Thr	Asp	Ala	Туг	Thr 60	Leu	Ser	Gly	Ala
Asp 65	Pro	Glu	Gly	Cys	Phe 70	Pro	Val	Ile	Leu	Gly 75	His	Glu	Gly	Ala	Gly 80
Ile	Val	Glu	Ser	Val 85	Gly	Glu	Gly	Val	Thr 90	Lys	Leu	Lys	Ala	Gly 95	Asp
Thr	Val	Ile	Pro 100	Leu	Tyr	Ile	Pro	Gln 105	Cys	Gly	Glu	Cys	Lys 110	Phe	Cys
Leu	Asn	Pro 115	Lys	Thr	Asn	Leu	Cys 120	Gln	Lys	Ile	Arg	Val 125	Thr	Gln	Gly
Lys	Gly 130	Leu	Met	Pro	Asp	Gly 135	Thr	Ser	Arg	Phe	Thr 140	Cys	Lys	Gly	Lys
Thr 145	Ile	Leu	His	Tyr	Met 150	Gly	Thr	Ser	Thr	Phe 155	Ser	Glu	Tyr	Thr	Val 160
Val	Ala	Asp	Ile	Ser 165	V al	Ala	Lys	Ile	Asp 170	Pro	Leu	Ala	Pro	Leu 175	Asp
Lys	Val	Cys	Leu 180	Leu	Gly	Cys	Gly	Ile 185	Ser	Thr	Gly	Tyr	Gly 190	Ala	Ala
Val	Asn	Thr 195	Ala	Lys	Leu	Glu	Pro 200	Gly	Ser	Val	Cys	Ala 205	Val	Phe	Gly
Leu	Gly 210	Gly	Val	Gly	Leu	Ala 215	Val	Ile	Met	Gly	Cys 220	Lys	Val	Ala	Gly
Ala 225	Ser	Aṛg	Ile	Ile	Gly 230	Val	Asp	Ile	Asn	Lys 235	Asp	Lys	Phe	Ala	Arg 240
Ala	Lys	Glu	Phe	Gly 245	Ala	Thr	Glu	Суз	Ile 250	Asn	Pro	Gln	Asp	Phe 255	Ser
Lys	Pro	Ile	Gln 260	Glu	Val	Leu	Ile	Glu 265	Met	Thr	Asp	Gly	Gly 270	Val	Asp
Tyr	Ser	Phe 275	Glu	Cys	Ile	Gly	Asn 280	Val	Lys	Val	Met	Arg 285	Ala	Ala	Leu
Glu	Ala	Cys	His	Lys	Gly	Trp	Gly	Val	Thr	Xaa	Val	Val	Gly	Val	Ala

796

Ala Ser Gly Glu Glu Ile Ala Thr Arg Pro Phe Gln Leu Val Thr Gly 305 310 315 320

Arg Thr Trp Lys Gly Thr Ala Phe Gly Gly Trp Lys Ser Val Glu Ser 325 330 335

Val Pro Lys Leu Val Ser Glu Tyr Met Ser Lys Lys Ile Lys Val Asp 340 345 350

Glu Phe Val Thr His Asn Leu Ser Phe Asp Glu Ile Asn Lys Ala Phe 355 360 365

Glu Leu Met His Ser Gly Lys Ser Ile Arg Thr Val Val Lys Ile 370 375 380

<210> 851

<211> 154

<212> PRT

<213> Homo sapiens

<400> 851

Ala Arg Ala Pro Arg Ala Thr Leu Asn Gly Pro Gly Ala Arg Gly Arg

1 10 15

Val Gly Val Val Leu Arg Pro Arg Pro Arg Gly Leu Arg Phe Pro 20 25 30

Trp Cys Pro Gly Arg Pro Ala Ser Gly Ala Val Ser Tyr Glu Ser Ala 35 40 45

His Ala Ala Ser Val Arg Leu Thr Leu Arg Thr Met Glu Gly Gly Phe 50 55 60

Gly Ser Asp Phe Gly Gly Ser Gly Ser Gly Lys Leu Asp Pro Gly Leu 65 70 75 80

Ile Met Glu Gln Val Lys Val Gln Ile Ala Val Ala Asn Ala Gln Glu
85 90 95

Leu Leu Gln Arg Met Thr Asp Lys Cys Phe Arg Lys Cys Ile Gly Lys
100 105 110

Pro Gly Gly Ser Leu Asp Asn Ser Glu Gln Lys Cys Ile Ala Met Cys 115 120 125

Met Asp Arg Tyr Met Asp Ala Trp Asn Thr Val Ser Arg Ala Tyr Asn 130 135 140

Ser Arg Leu Gln Arg Glu Arg Ala Asn Met

797

•

150

145

210

<210> 852 <211> 396 <212> PRT <213> Homo sapiens <400> 852 Asp Ser Arg Val Asp Pro Arg Val Arg Ala Ile Ile Ala Lys Thr Phe Lys Gly Arg Gly Ile Thr Gly Val Glu Asp Lys Glu Ser Trp His Gly Lys Pro Leu Pro Lys Asn Met Ala Glu Gln Ile Ile Gln Glu Ile Tyr Ser Gln Ile Gln Ser Lys Lys Ile Leu Ala Thr Pro Pro Gln Glu Asp Ala Pro Ser Val Asp Ile Ala Asn Ile Arg Met Pro Ser Leu Pro Ser Tyr Lys Val Gly Asp Lys Ile Ala Thr Arg Lys Ala Tyr Gly Gln Ala Leu Ala Lys Leu Gly His Ala Ser Asp Arg Ile Ile Ala Leu Asp Gly Asp Thr Lys Asn Ser Thr Phe Ser Glu Ile Phe Lys Lys Glu His Pro Asp Arg Phe Ile Glu Cys Tyr Ile Ala Glu Gln Asn Met Val Ser Ile Ala Val Gly Cys Ala Thr Arg Asn Arg Thr Val Pro Phe Cys Ser 150 155 Thr Phe Ala Ala Phe Phe Thr Arg Ala Phe Asp Gln Ile Arg Met Ala

Ala Ile Ser Glu Ser Asn Ile Asn Leu Cys Gly Ser His Cys Gly Val

Ser Ile Gly Glu Asp Gly Pro Ser Gln Met Ala Leu Glu Asp Leu Ala

Met Phe Arg Ser Val Pro Thr Ser Thr Val Phe Tyr Pro Ser Asp Gly

215

Val Ala Thr Glu Lys Ala Val Glu Leu Ala Ala Asn Thr Lys Gly Ile 230 235 Cys Phe Ile Arg Thr Ser Arg Pro Glu Asn Ala Ile Ile Tyr Asn Asn 250 245 Asn Glu Asp Phe Gln Val Gly Gln Ala Lys Val Val Leu Lys Ser Lys 265 Asp Asp Gln Val Thr Val Ile Gly Ala Gly Val Thr Leu His Glu Ala 280 Leu Ala Ala Ala Glu Leu Leu Lys Lys Glu Lys Ile Asn Ile Arg Val 300 295 Leu Asp Pro Phe Thr Ile Lys Pro Leu Asp Arg Lys Leu Ile Leu Asp 305 310 315 Ser Ala Arg Ala Thr Lys Gly Arg Ile Leu Thr Val Glu Asp His Tyr 325 330 Tyr Glu Gly Gly Ile Gly Glu Ala Val Ser Ser Ala Val Val Gly Glu 340 345 Pro Gly Ile Thr Val Thr His Leu Ala Val Asn Arg Val Pro Arg Ser 360 Gly Lys Pro Ala Glu Leu Leu Lys Met Phe Gly Ile Asp Arg Asp Ala 375 Ile Ala Gln Ala Val Arg Gly Leu Ile Thr Lys Ala 385 390 <210> 853 <211> 302 <212> PRT <213> Homo sapiens <220>

<223> Xaa equals any of the naturally occurring L-amino acids
<400> 853
Ser Arg Leu Gly Leu Gln Ser Cys Gly Leu Ser Thr Gln Ala Ile Thr
1 5 10 15

Leu Ser Glu Thr Ala Ala Leu Asp Cys Ser Leu Pro Arg Leu His

<221> SITE <222> (228)

			20					25					30		
Ala	Arg	Gln 35	Ser	Met	Arg	Val	Thr 40	Leu	Ala	Thr	Ile	Ala 45	Trp	Met	Val
Ser	Phe 50	Val	Ser	Asn	Tyr	Ser 55	His	Thr	Ala	Asn	Ile 60	Leu	Pro	Asp	Ile
Glu 65	Asn	Glu	Asp	Phe	Ile 70	Lys	Asp	Cys	Val	Arg 75	Ile	His	Asn	Lys	Phe 80
Arg	Ser	Glu	Val	Lys 85	Pro	Thr	Ala	Ser	Asp 90	Met	Leu	Tyr	Met	Thr 95	Trp
Asp	Pro	Ala	Leu 100	Ala	Gln	Ile	Ala	Lys 105	Ala	Trp	Ala	Ser	Asn 110	Суз	Gln
Phe	Ser.	His 115	Asn	Thr	Arg	Leu	Lys 120	Pro	Pro	His		Leu 125	His	Pro	Asn
Phe	Thr 130	Ser	Leu	Gly	Glu	Asn 135	Ile	Trp	Thr	Gly	Ser 140	Val	Pro	Ile	Phe
Ser 145	Val	Ser	Ser	Ala	11e 150	Thr	Asn	Trp	Tyr	Asp 155	Glu	Ile	Gln	Asp	Туг 160
Asp	Phe	Lys	Thr	Arg 165	Ile	Cys	Lys	Lys	Val 170	Суз	Gly	His	Tyr	Thr 175	Gln
Val	Val	Trp	Ala 180	Asp	Ser	Tyr	Lys	Val 185	Gly	Cys	Ala	Val	Gln 190	Phe	Cys
Pro	Lys	Val 195	Ser	Gly	Phe	Asp	Ala 200	Leu	Ser	Asn	Gly	Ala 205	His	Phe	Ile
Cys	Asn 210	Tyr	Gly	Pro	Gly	Gly 215	Asn	Tyr	Pro	Thr	Trp 220	Pro	Tyr	Lys	Arg
31y 225	Ala	Thr	Xaa	Ser	Ala 230	Суѕ	Pro	Asn	Asn	Asp 235	Lys	Суѕ	Leu	Asp	Asn 240
Leu	Cys	Val	Asn	Arg 245	Gln	Arg	Asp	Gln	Val 250	Lys	Arg	Tyr	Tyr	Ser 255	Val
/al	Tyr	Pro	Gly 260	Trp	Pro	Ile	Tyr	Pro 265	Arg	Asn	Arg	Tyr	Thr 270	Ser	Leu
he?	Leu	Ile 275	Val-	Asn	Ser	Val	Ile 280	Leu	Ile	Leu	Ser	Val 285	Ile	Ile	Thr
le	Leu	Val	Gln	His	Lvs	Tvr	Pro	Asn	Leu	Val	Leu	Leu	Asp		

800

290 295 300

<210> 854 <211> 237 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (235)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 854

Val Pro Ala Ser Phe Ala Ala Ala Ser Ala Val Leu Ser Ala Val Phe

1 5 10 15

Pro Gln Glu Pro Ala Tyr Phe Leu Asn Met Glu Ser Val Val Arg Arg

Cys Pro Phe Leu Ser Arg Val Pro Gln Ala Phe Leu Gln Lys Ala Gly
35 40 45

Lys Ser Leu Leu Phe Tyr Ala Gln Asn Cys Pro Lys Met Met Glu Val 50 55 60

Gly Ala Lys Pro Ala Pro Arg Ala Leu Ser Thr Ala Ala Val His Tyr 65 70 75. 80

Gln Gln Ile Lys Glu Thr Pro Pro Ala Ser Glu Lys Asp Lys Thr Ala 85 90 95

Lys Ala Lys Val Gln Gln Thr Pro Asp Gly Ser Gln Gln Ser Pro Asp 100 105 110

Gly Thr Gln Leu Pro Ser Gly His Pro Leu Pro Ala Thr Ser Gln Gly
115 120 125

Thr Ala Ser Lys Cys Pro Phe Leu Ala Ala Gln Met Asn Gln Arg Gly
130 135 140

Ser Ser Val Phe Cys Lys Ala Ser Leu Glu Leu Gln Glu Asp Val Gln 145 150 155 160

Glu Met Asn Ala Val Arg Lys Glu Val Ala Glu Thr Ser Ala Gly Pro 165 170 175

Ser Val Val Ser Val Lys Thr Asp Gly Gly Asp Pro Ser Gly Leu Leu 180 185 190

Lys Asn Phe Gln Asp Ile Met Gln Lys Gln Arg Pro Glu Arg Val Ser 195 200 205

His Leu Leu Gln Asp Asn Leu Pro Lys Ser Val Ser Thr Phe Gln Tyr 210 215 220

Asp Arg Phe Phe Glu Lys Lys Ile Asp Glu Xaa Lys Glu 225 230 235

<210> 855

<211> 272

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (202)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 855

Thr Pro Gly Ile Phe Thr Glu Gln Ser Met Ile Thr Phe Leu Pro Leu
1 5 10 15

Leu Leu Gly Leu Ser Leu Gly Cys Thr Gly Ala Gly Gly Phe Val Ala 20 25 30

His Val Glu Ser Thr Cys Leu Leu Asp Asp Ala Gly Thr Pro Lys Asp 35 40 45

Phe Thr Tyr Cys Ile Ser Phe Asn Lys Asp Leu Leu Thr Cys Trp Asp

50 55 60

Pro Glu Glu Asn Lys Met Ala Pro Cys Glu Phe Gly Val Leu Asn Ser 65 70 75 80

Leu Ala Asn Val Leu Ser Gln His Leu Asn Gln Lys Asp Thr Leu Met 85 90 95

Gln Arg Leu Arg Asn Gly Leu Gln Asn Cys Ala Thr His Thr Gln Pro 100 105 110

Phe Trp Gly Ser Leu Thr Asn Arg Thr Arg Pro Pro Ser Val Gln Val 115 120 125

Ala Lys Thr Thr Pro Phe Asn Thr Arg Glu Pro Val Met Leu Ala Cys 130 135 140

Tyr Val Trp Gly Phe Tyr Pro Ala Glu Val Thr Ile Thr Trp Arg Lys 145 150 155 160

Asn	Gly	Lys	Leu	Val 165	Met	Pro	His	Ser	Ser 170	Ala	His	Lys	Thr	Ala 175	Glı
Pro	Asn	Gly	Asp 180	Trp	Thr	Tyr	Gln	Thr 185	Leu	Ser	His	Leu	Ala 190	Leu	Thi
Pro	Ser	Туг 195	Gly	Asp	Thr	Tyr	Thr 200	Cys	Xaa	Val	Glu	His 205	Ile	Gly	Ala
Pro	Glu 210	Pro	Ile	Leu	Arg	Asp 215	Trp	Thr	Ρ̀το	Gly	Leu 220	Ser	Pro	Met	Glr
Thr 225	Leu	Lys	Val	Ser	Val 230	Ser	Ala	Val	Thr	Leu 235	Gly	Leu	Gly	Leu	11e 240
Ile	Phe	Ser	Leu	Gly 245	Val	Ile	Ser	Trp	Arg 250	Arg	Ala	Gly	His	Ser 255	Sei
Tyr	Thr	Pro	Leu 260	Pro	Gly	Ser	Asn	Tyr 265	Ser	Glu	Gly	Trp	His 270	Ile	Ser

<210> 856

<211> 153

<212> PRT

<213> Homo sapiens

<400> 856

Val Val Ala Arg Phe Ile Arg Ile Tyr Pro Leu Thr Trp Asn Gly Ser 1 5 10 15

Leu Cys Met Arg Leu Glu Val Leu Gly Cys Ser Val Ala Pro Val Tyr
20 25 30

Ser Tyr Tyr Ala Gln Asn Glu Val Val Ala Thr Asp Asp Leu Asp Phe 35 40 45

Arg His His Ser Tyr Lys Asp Met Arg Gln Leu Met Lys Val Val Asn 50 55 60

Glu Glu Cys Pro Thr Ile Thr Arg Thr Tyr Ser Leu Gly Lys Ser Ser 65 70 75 80

Arg Gly Leu Lys Ile Tyr Ala Met Glu Ile Ser Asp Asn Pro Gly Glu 85 90 95

His Glu Leu Gly Glu Pro Glu Phe Arg Tyr Thr Ala Gly Ile His Gly 100 105 110

Asn Glu Val Leu Gly Arg Glu Leu Leu Leu Leu Leu Met Gln Tyr Leu 115 120 125

Cys Arg Glu Tyr Arg Asp Gly Asn Pro Arg Val Arg Ser Trp Cys Arg 130 135 140

Thr His Ala Ser Thr Trp Cys Pro His 145 150

<210> 857

<211> 258

<212> PRT

<213> Homo sapiens

<400> 857

Cys Leu Ser Gln Lys Ala Val Arg Ala Pro Arg Phe Leu Arg Gly Leu
1 5 10 15

Pro Ser Gly Arg Val Asn Cys Phe Leu Gln Ala Gly His Gly Ala Ser 20 25 30

Arg Ser Gln Gly Ser Gly Leu Cys Gln Met Leu Lys Glu Gly Ala Lys
35 40 45

His Phe Ser Gly Leu Glu Glu Ala Val Tyr Arg Asn Ile Gln Ala Cys 50 55 60

Lys Glu Leu Ala Gln Thr Thr Arg Thr Ala Tyr Gly Pro Asn Gly Met 65 70 75 80

Asn Lys Met Val Ile Asn His Leu Glu Lys Leu Phe Val Thr Asn Asp 85 90 95

Ala Ala Thr Ile Leu Arg Glu Leu Glu Val Gln His Pro Ala Ala Lys
100 105 110

Met Ile Val Met Ala Ser His Met Gln Glu Gln Glu Val Gly Asp Gly
115 120 125

Thr Asn Phe Val Leu Val Phe Ala Gly Ala Leu Leu Glu Leu Ala Glu 130 135 140

Glu Leu Leu Arg Ile Gly Leu Ser Val Ser Glu Val Ile Glu Gly Tyr 145 150 155 160

Glu Ile Ala Cys Arg Lys Ala His Glu Ile Leu Pro Asn Leu Val Cys

804

165 170 175 Cys Ser Ala Lys Asn Leu Arg Asp Ile Asp Glu Val Ser Ser Leu Leu 180 185 Arg Thr Ser Ile Met Ser Lys Gln Tyr Gly Asn Glu Val Phe Leu Ala 200 Lys Leu Ile Ala Gln Ala Cys Val Ser Ile Phe Pro Asp Ser Gly His 215 Phe Asn Val Asp Asn Ile Arg Val Cys Lys Ile Leu Gly Ser Gly Ile 225 235 Ser Ser Ser Val Leu His Gly Met Val Phe Lys Lys Glu Thr Glu 245 Val Met <210> 858 <211> 143 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (14) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (135) <223> Xaa equals any of the naturally occurring L-amino acids Pro Asp Ser Leu Pro Pro Pro Ser Pro Arg Leu Pro Ala Xaa Gly Pro Glu Phe Pro Gly Arg Pro Thr Arg Pro Glu Arg Ser Pro Ser Leu Gly 25 Ile Pro Lys Cys Phe His Ser Val Ile Arg Thr Glu His Arg Gly Leu 40 35

Thr Met Glu Phe Gly Leu Ser Trp Ile Phe Leu Ala Ala Ile Leu Lys

Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val

65 70 75 80 Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr 90 Phe Ser Asn Ala Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly 100 105 Leu Glu Trp Val Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala Pro Val Xaa Arg Gln Ile His His Leu Lys Arg 130 135 <210> 859 <211> 135 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (132) <223> Kaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (133) <223> Xaa equals any of the naturally occurring L-amino acids <400> 859 Val Thr Met Ala Gln Gln Ala Ala Asp Lys Tyr Leu Tyr Val Asp Lys Asn Phe Ile Asn Asn Pro Leu Ala Gln Ala Asp Trp Ala Ala Lys Lys 30 20 Leu Val Trp Val Pro Ser Asp Lys Ser Gly Phe Glu Pro Ala Ser Leu 40 Lys Glu Glu Val Gly Glu Glu Ala Ile Val Glu Leu Val Glu Asn Gly 55 Lys Lys Val Lys Val Asn Lys Asp Asp Ile Gln Lys Met Asn Pro Pro 65 Lys Phe Ser Lys Val Glu Asp Met Ala Glu Leu Thr Cys Leu Asn Glu

Ala Ser Val Leu His Asn Leu Lys Glu Arg Tyr Tyr Ser Gly Leu Ile

806

100 105 110 Tyr Val Ser Gly Cys Arg Gly Thr Pro Gln Ala Gly Ser Glu Gly Ser 115 120 Glu Val Gly Xaa Xaa Ala Gly 130 135 <210> 860 <211> 52 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (2) <223> Xaa equals any of the naturally occurring L-amino acids <400> 860 Ala Xaa Leu Ile Lys Thr Arg Val Leu Ile Tyr Asn Lys Ser Asn Phe 10 Ser Leu Ser Leu Gly Thr Ser Asn Cys Thr Pro Gln Ile Thr Asp Thr 20 25 Ser Glu Phe Phe Met Val Lys Lys Ala Pro Thr Leu Thr Tyr Lys Cys 35 40 Gly Pro Arg Asn 50 <210> 861 <211> 321 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (18) <223> Xaa equals any of the naturally occurring L-amino acids

Ala His Gly Val Thr Ser Ala Pro Asp Asn Arg Pro Ala Leu Gly Ser

Thr Xaa Pro Pro Val His Asn Val Thr Ser Ala Ser Gly Ser Ala Ser

25

10

15

30

5

20

<400> 861

GIY	SEL	35	ser	Int	rea	Val	40	ASII	Gly	TIIL	Ser	45	ALG	MIG	THE
Thr	Thr 50	Pro	Ala	Ser	Lys	Ser 55	Thr	Pro	Phe	Ser	Ile 60	Pro	Ser	His	His
Ser 65	Asp	Thr	Pro	Thr	Thr 70	Leú	Ala	Ser	His	Ser 75	Thr	Lys	Thr	Asp	Ala 80
Ser	Ser	Thr	His	His 85	Ser	Thr	Val	Pro	Pro 90	Ĺeu	Thr	Ser	Ser	Asn 95	His
Ser	Thr	Ser	Pro 100	Gln	Leu	Ser	Thr	Gly 105	Val	Ser	Phe	Phe	Phe 110	Leu	Ser
Phe	His	11e 115	Ser	Asn	Leu	Gln	Phe 120	Asn	Ser	Ser	Leu	Glu 125	ysb	Pro	Ser
Thr	Asp 130	Tyr	Tyr	Gln	Glu	Leu 135	Gln	Arg	Asp	Ile	Ser 140	Glu	Met	Phe	Leu
Gln 145	Ile	Tyr	Lys	Gln	Gly 150	Gly	Phe	Leu	Gly	Leu 155	Ser	Asn	Ile	Lys	Phe 160
Arg	Pro	Gly	Ser	Val 165	Val	Val	Gln	Leu	Thr 170	Leu	Ala	Phe	Arg	Glu 175	Gly
Thr	Ile	Asn	Val 180	His	Asp	Val	Glu	Thr 185	Gln	Phe	Asn	Gln	Туг 190	Lys	Thr
Glu	Ala	Ala 195	Ser	Arg	Tyr	Asn	Leu 200	Thr	Ile	Ser	Asp	Val 205	Ser	Val	Ser
Asp	Val 210	Pro	Phe	Pro	Phe	Ser 215	Ala	Gln	Ser	Gly	Ala 220	Gly	Val	Pro	Gly
Trp 225	Gly	Ile	Ala	Leu	Leu 230	Val	Leu	Val	Cys	Val 235	Leu	Val	Ala	Leu ⁄	Ala 240
Ile	Val	Tyr	Leu	Ile 245	Ala	Leu	Ala	Val	Cys 250		Cys	Arg	Arg	Lys 255	Asn
Tyr	Gly	Gln	Leu 260	Asp	Ile	Phe	Pro	Ala 265	Arg	Asp	Thr	Tyr	His 270	Pro	Met
Ser	Glu	Туг 275	Pro	Thr	Tyr	His	Thr 280	His	Gly	Arg	Tyr	Val 285	Pro	Pro	Ser
Ser	Thr 290	Asp	Arg	Ser		Tyr 295	Glu	Lys	Val	Ser	Ala 300	Gly	Asn	Gly	Gly

Ser Ser Leu Ser Tyr Thr Asn Pro Ala Val Ala Ala Thr Ser Ala Asn 305 310 315 Leu <210> 862 <211> 327 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (307) <223> Kaa equals any of the naturally occurring L-amino acids <400> 862 Phe Gly Thr Ser Leu Thr Gln Val Leu Leu Gly Ala Gly Glu Asn Thr Lys Thr Asn Leu Glu Ser Ile Leu Ser Tyr Pro Lys Asp Phe Thr Cys 25

Ser Gln Ile Phe His Ser Pro Asp Leu Ala Ile Arg Asp Thr Phe Val

Val His Gln Ala Leu Lys Gly Phe Thr Thr Lys Gly Val Thr Ser Val 35 40 45

Asn Ala Ser Arg Thr Leu Tyr Ser Ser Ser Pro Arg Val Leu Ser Asn

Asn Ser Asp Ala Asn Leu Glu Leu Ile Asn Thr Trp Val Ala Lys Asn 85 90 95

Thr Asn Asn Lys Ile Ser Arg Leu Leu Asp Ser Leu Pro Ser Asp Thr 100 105 110

Arg Leu Val Leu Leu Asn Ala Ile Tyr Leu Ser Ala Lys Trp Lys Thr 115 120 125

Thr Phe Asp Pro Lys Lys Thr Arg Met Glu Pro Phe His Phe Lys Asn 130 135 140

Ser Val Ile Lys Val Pro Met Met Asn Ser Lys Lys Tyr Pro Val Ala 145 150 155 160

His Phe Ile Asp Gln Thr Leu Lys Ala Lys Val Gly Gln Leu Gln Leu

809

170

Ser His Asn Leu Ser Leu Val Ile Leu Val Pro Gln Asn Leu Lys His

175.

165

180 185 Arg Leu Glu Asp Met Glu Gln Ala Leu Ser Pro Ser Val Phe Lys Ala 200 195 Ile Met Glu Lys Leu Glu Met Ser Lys Phe Gln Pro Thr Leu Leu Thr Leu Pro Arg Ile Lys Val Thr Thr Ser Gln Asp Met Leu Ser Ile Met 235 Glu Lys Leu Glu Phe Phe Asp Phe Ser Tyr Asp Leu Asn Leu Cys Gly Leu Thr Glu Asp Pro Asp Leu Gln Val Ser Ala Met Gln His Gln Thr 265 Val Leu Glu Leu Thr Glu Thr Gly Val Glu Ala Ala Ala Ala Ser Ala 280 Ile Ser Val Ala Arg Thr Leu Leu Val Phe Glu Val Gln Gln Pro Phe 295 Leu Phe Xaa Leu Trp Asp Gln Gln His Lys Phe Pro Val Phe Met Gly 310 315 Arg Val Tyr Asp Pro Arg Ala 325 <210> 863 <211> 86 <212> PRT <213> Homo sapiens <400> 863 Tyr Tyr Ile Val His Leu Lys Leu Thr Glu Arg Val Asn Leu Lys Cys 5 10 Ser His His Thr Asn Pro Lys Val Thr Met Phe Ser Pro His Lys Pro Lys Gly Asn Tyr Val Leu Ile Ser Leu Ile Val Val Thr Ile Ser Gln Cys Ile His Leu Pro Lys His Tyr Val Val Tyr Leu Glu Tyr Ile Ile

Leu Phe Ile Asn Tyr Thr Ser Ile Lys Leu Lys Glu Gly Ile Thr Asn 65 70 75 80

Ser His Lys Ile Gln Ile 85

<210> 864

<211> 130

<212> PRT

<213> Homo sapiens

<400> 864

Leu Thr Gln Gln Gln Fro Ala Thr Gly Pro Gln Pro Ser Leu Gly
1 5 10 15

Val Ser Phe Gly Thr Pro Phe Gly Ser Gly Ile Gly Thr Gly Leu Gln
20 25 30

Ser Ser Gly Leu Gly Ser Ser Asn Leu Gly Gly Phe Gly Thr Ser Ser 35 40 45

Gly Phe Gly Cys Ser Thr Thr Gly Ala Ser Thr Phe Gly Phe Gly Thr
50 55 60

Thr Asn Lys Pro Ser Gly Ser Leu Ser Ala Gly Phe Gly Ser Ser Ser 65 70 75 80

Thr Ser Gly Phe Asn Phe Ser Asn Pro Gly Ile Thr Ala Ser Ala Gly 85 90 95

Leu Thr Phe Gly Val Ser Asn Pro Ala Ser Ala Gly Phe Gly Thr Gly 100 105 110

Gly Gln Leu Leu Gln Leu Lys Lys Pro Pro Ala Gly Asn Lys Arg Gly
115 120 125

Lys Arg 130

<210> 865

<211> 78

<212> PRT

<213> Homo sapiens

<400> 865

Ser Glu Trp Lys Ile Lys Gly Pro Ser Ser Pro Leu Ala Ser Leu Pro

1 10 Gly Arg Arg His Gly Gly Ser Ser Ala Thr Gly Ala Cys Gly Glu Ala Met Ala Ala Glu Gly Ser Ser Gly Pro Ala Gly Leu Thr Leu Gly 40 Arg Ser Phe Ser Asn Tyr Arg Pro Phe Glu Pro Gln Ala Leu Gly Leu Ser Pro Ser Trp Arg Leu Thr Gly Phe Ser Gly Met Lys Gly <210> 866 <211> 529 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (8) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (517) <223> Xaa equals any of the naturally occurring L-amino acids <400> 866 Pro Pro Pro Glu Pro Arg Ala Xaa Met Ala Glu Asn Pro Ser Leu Glu Asn His Arg Ile Lys Ser Phe Lys Asn Lys Gly Arg Asp Val Glu Thr 20 Met Arg Arg His Arg Asn Glu Val Thr Val Glu Leu Arg Lys Asn Lys 40 Arg Asp Glu His Leu Leu Lys Lys Arg Asn Val Pro Gln Glu Glu Ser Leu Glu Asp Ser Asp Val Asp Ala Asp Phe Lys Ala Gln Asn Val Thr 65 70 Léu Glu Ala Ile Leu Gln Asn Ala Thr Ser Asp Asn Pro Val Val Gln Leu Ser Ala Val Gln Ala Ala Arg Lys Leu Leu Ser Ser Asp Arg Asn

			100					105					110		
Pro	Pro	Ile 115	Asp	Asp	Leu	Ile	Lys 120	Ser	Gly	Ile	Leu	Pro 125	Ile	Leu	Val
Lys	Cys 130	Leu	Glu	Arg	Asp	Asp 135	Asn	Pro	Ser	Leu	Gln 140	Phe	Glu	Ala	Ala
Trp 145	Ala	Leu	Thr	Asn	Ile 150	Ala	Ser	Gly	Thr	Ser 155	Ala	Gln	Thr	Gln	Ala 160
Val	Val	Gln	Ser	Asn 165	Ala	Val	Pro	Leu	Phe 170	Leu	Arg	Leu	Leu	Arg 175	Ser
Pro	His	Gln	Asn 180	Val	Суз	Glu	Gln	Ala 185	Val	Trp	Ala	Leu	Gly 190	Asn	Ile
Ile	Gly	Asp 195	Gly	Pro	Gln	Cys	Arg 200	Asp	Tyr	Val	Ile	Ser 205	Leu	Gly	Val
Val	Lys 210	Pro	Leu	Leu	Ser	Phe 215	Ile	Ser	Pro	Ser	Ile 220	Pro	Ile	Thr	Phe
Leu 225	Arg	Asn	Val	Thr	Trp 230	Val	Ile	Val	Asn	Leu 235	Cys	Arg	Asn	Lys	Asp 240
Pro	Pro	Pro	Pro	Met 245	Glu	Thr	Val	Gln	Glu 250	Ile	Leu	Pro	Ala	Leu 255	Сув
Val	Leu	Ile	Туг 260	His	Thr	Asp	Ile	Asn 265	Ile	Leu	Val	Asp	Thr 270	Val	Trp
Ala	Leu	Ser 275	Tyr	Leu	Thr	Asp	Gly 280	Gly	Asn	Glu	Gln	Ile 285	Gln	Met	Val
Ile	Asp 290	Ser	Gly	Val	Val	Pro 295	Phe	Leu	Val	Pro	Leu 300	Leu	Ser	His	Gln
Glu 305	Val	Lys	Val	Gln	Thr 310	Ala	Ala	Leu	Arg	Ala 315	Val	Gly	Asn	Ile	Val 320
Thr	Gly	Thr	Asp	Glu 325	Gln	Thr	Gln	Val	Val 330	Leu	Asn	Cys	Asp	Val 335	Leu
Ser	His	Phe	Pro 340	Asn	Leu	Leu	Ser	His 345	Pro	Lys	Glu	Lys	Ile 350	Asn	Lys
Glu	Ala	Val 355	Trp	Phe	Leu	Ser	Asn 360	Ile	Thr	Ala	Gly	Asn 365	Gln	Gln	Gln
Va l	Gln	Ala	Val	Ile	Asp	Ala	Glv	Leu	Ile	Pro	Met	Ile	Ile	His	Gln

813

380

375

370

Leu Ala Lys Gly Asp Phe Gly Thr Gln Lys Glu Ala Ala Trp Ala Ile 395 390 Ser Asn Leu Thr Ile Ser Gly Arg Lys Asp Gln Val Glu Tyr Leu Val 405 Gln Gln Asn Val Ile Pro Pro Phe Cys Asn Leu Leu Ser Val Lys Asp Ser Gln Val Val Gln Val Val Leu Asp Gly Leu Lys Asn Ile Leu Ile 435 440 Met Ala Gly Asp Glu Ala Ser Thr Ile Ala Glu Ile Ile Glu Glu Cys Gly Gly Leu Glu Lys Ile Glu Val Leu Gln Gln His Glu Asn Glu Asp 470 475 Ile Tyr Lys Leu Ala Phe Glu Ile Ile Asp Gln Tyr Phe Ser Gly Asp 485 Asp Ile Asp Glu Asp Pro Cys Leu Ile Pro Glu Ala Thr Gln Gly Gly 505 Thr Tyr Asn Phe Xaa Pro Thr Ala Asn Leu Gln Thr Lys Glu Phe Asn 520 Phe <210> 867 <211> 237 <212> PRT <213> Homo sapiens <400> 867 Arg Pro Gly Pro Val Arg Arg Gly Lys Val Glu Leu Ile Lys Phe 5 Val Arg Val Gln Trp Arg Arg Pro Gln Val Glu Trp Arg Arg Arg Arg 25 Trp Gly Pro Gly Pro Gly Ala Ser Met Ala Gly Ser Glu Glu Leu Gly 35

Leu Arg Glu Asp Thr Leu Arg Val Leu Ala Ala Phe Leu Arg Arg Gly

Glu Ala Ala Gly Ser Pro Val Pro Thr Pro Pro Arg Ser Pro Ala Gln

Glu Glu Pro Thr Asp Phe Leu Ser Arg Leu Arg Arg Cys Leu Pro Cys

Ser Leu Gly Arg Gly Ala Ala Pro Ser Glu Ser Pro Arg Pro Cys Ser 100

Leu Pro Ile Arg Pro Cys Tyr Gly Leu Glu Pro Gly Pro Ala Thr Pro 120

Asp Phe Tyr Ala Leu Val Ala Gln Arg Leu Glu Gln Leu Val Gln Glu 135

Gln Leu Lys Ser Pro Pro Ser Pro Glu Leu Gln Gly Pro Pro Ser Thr 150

Glu Lys Glu Ala Ile Leu Arg Arg Leu Val Ala Leu Leu Glu Glu Glu 170

Ala Glu Val Ile Asn Gln Lys Leu Ala Ser Asp Pro Ala Leu Arg Thr

Ser Trp Ser Ala Cys Pro Pro Thr Leu Ser Pro Ala Trp Trp Ser Cys 200

Ser Val Ala Gly Met Thr Ala Leu Ala Gln Ala Glu His Ala Pro Gly 215

Pro Arg Leu Leu Pro Arg Ser Pro Trp Pro Ala Trp Pro 225 230

<210> 868

<211> 196

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (9)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 8	36	8
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Leu Ser Val Ser Ala Xaa Ala Ala Xaa Val Ala Ala Ala Ala Ile His 1 5 10 15

Ser Asp Ser Ala Ala Ala Pro Gly Gly Gly Ala Ala Arg Asp Phe 20 25 30

Phe Phe Gln Thr Asp Arg Gly Ala Ala Ala Asp Met Ser Thr Pro 35 40 45

Ala Arg Arg Arg Leu Met Arg Asp Phe Lys Arg Leu Gln Glu Asp Pro 50 55 60

Pro Val Gly Val Ser Gly Ala Pro Ser Glu Asn Asn Ile Met Gln Trp
65 70 75 80

Asn Ala Val Ile Phe Gly Pro Glu Gly Thr Pro Phe Glu Asp Gly Thr 85 90 95

Phe Lys Leu Val Ile Glu Phe Ser Glu Glu Tyr Pro Asn Lys Pro Pro 100 105 110

Thr Val Arg Phe Leu Ser Lys Met Phe His Pro Asn Val Tyr Ala Asp 115 120 125

Gly Ser Ile Cys Leu Asp Ile Leu Gln Asn Arg Trp Ser Pro Thr Tyr 130 135 140

Asp Val Ser Ser Ile Leu Thr Ser Ile Gln Ser Leu Leu Asp Glu Pro 145 150 155 160

Asn Pro Asn Ser Pro Ala Asn Ser Gln Ala Ala Gln Leu Tyr Gln Glu 165 170 175

Asn Lys Arg Glu Tyr Glu Lys Arg Val Ser Ala Ile Val Glu Gln Ser 180 185 190

Trp Asn Asp Ser 195

<210> 869

<211> 544

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (7)

<223> Xaa equals any of the naturally occurring L-amino acids

<220)>														
<22	l> si	ITE													
	?> (9										_		_		_
<223	3> Xa	aa e	quals	any	of	the	nati	ırall	Ly o	curi	ring	L-an	nino	acio	is
<400)> 86	59													
			Trp	Val	Ala	Xaa	Ala	Xaa	Ala	Ser	Ser	Gly	Leu	Val	Val
1	-		_	5					10					15	
										_		_			_
Ala	Arg	Pro		Ser	Ala	Val	Pro		Glu	Pro	Arg	Pro	Phe 30	Arg	Pro
			20					25					30		
Ser	Pro	Pro	His	Leu	Ala	Ala	Met	Arg	Leu	Arg	Arg	Leu	Ala	Leu	Phe
		35					40					45			
			_								_				
Pro		Val	Ala	Leu	Leu		Ala	Ala	Ala	Arg	Leu 60	Ala	ATA	Ala	ser
	50					55					00				
Asp	Val	Leu	Glu	Leu	Thr	Asp	Asp	Asn	Phe	Glu	Ser	Arg	Ile	Ser	Asp
65					70					75					80
			_	_									_	_	_
Thr	Gly	Ser	Ala	_	Leu	Met	Leu	Val		Phe	Phe	Ala	Pro	Trp 95	Cys
				85					90					95	
Gly	His	Cys	Lys	Arq	Leu	Ala	Pro	Glu	Tyr	Glu	Ala	Ala	Ala	Thr	Arg
-		-	100	_				105	_	•			110		
Leu	Lys	_	Ile	Val	Pro	Leu		Lys	Val	Asp	Cys		Ala	Asn	Thr
		115					120					125			
Asn	Thr	Cvs	Asn	Lvs	Tyr	Glv	Val	Ser	Glv	Tvr	Pro	Thr	Leu	Lys	Ile
	130	-7-		-1-	-2-	135		,		•	140			-	
	Arg	Asp	Gly	Glu	Glu	Ala	Gly	Ala	Tyr		Gly	Pro	Arg	Thr	
145					150					155					160
Asp	Glv	Ile	Val	Ser	His	Leu	Lvs	Lvs	Gln	Ala	Gly	Pro	Ala	Ser	Val
	1			165			-1-		170		•			175	
Pro	Leu	Arg		Glu	Glu	Glu	Phe	_	Lys	Phe	Ile	Ser		Lys	Asp
			180				٠	185					190		
Ala	Ser	Ile	Val	Glv	Phe	Phe	Asp	Asp	Ser	Phe	Ser	Glu	Ala	His	Ser
		195		1			200					205			
Glu		Leu	Lys	Ala	Ala		Asn	Leu	Arg	Asp		Tyr	Arg	Phe	Ala
	210					215					220				
His	Thr	Asn	Val	Glu	Ser	Leu	Val	Asn	Glu	Tyr	Asp	Asp	Asn	Gly	Glu
225				_	230					235	-	-		_	240

Gly	Ile	Ile	Leu	Phe 245	Arg	Pro	Ser	His	Leu 250	Thr	Asn	Lys	Phe	Glu 255	Asp
Lys	Thr	Val	Ala 260	Tyr	Thr	Glu	Gln	Lys 265	Met	Thr	Ser	Gly	Lys 270	Ile	Lys
Lys	Phe	Ile 275	Gln	Glu	Asn	Ile	Phe 280	Gly	Ile	Cys	Pro	His 285	Met	Thr	Glu
Asp	Asn 290	Lys	Asp	Leu	Ile	Gln 295	Gly	Lys	Asp	Leu	Leu 300	Ile	Ala	туr	Tyr
Asp 305	Val	Asp	Tyr	Glu	Lys 310	Asn	Ala	Lys	Gly	Ser 315	Asn	Tyr	Trp	Arg	Asn 320
Arg	Val	Met	Met	Val 325	Ala	Lys	Lys	Phe	Leu 330	Asp	Ala	Gly	His	Lys 335	Leu
Asn	Phe	Ala	Val 340	Ala	Ser	Arg	Lys	Thr 345	Phe	Ser	His	Glu	Leu 350	Ser	Asp
Phe	Gly	Leu 355	Glu	Ser	Thr	Ala	Gly 360	Glu	Ile	Pro	Val	Val 365	Ala	Ile	Arg
Thr	Ala 370	Lys	Gly	Glu	Lys	Phe 375	Val	Met	Gln	Glu	Glu 380	Phe	Ser	Arg	Asp
Gly 385	Lys	Ala	Leu	Glu	Arg 390	Phe	Leu	Gln	Asp	Tyr 395	Phe	Asp	Gly	Asn	Leu 400
Lys	Arg	Tyr	Leu	Lys 405	Ser	Glu	Pro	Ile	Pro 410	Glu	Ser	Asn	Asp	Gly 415	Pro
Val	Lys	Val	Val 420	Val	Ala	Glu	Asn	Phe 425	Asp	Glu	Ile	Val	Asn 430	Asn	Glu
Asn	Lys	Asp 435	Val	Leu	Ile	Glu	Phe 440	Tyr	Ala	Pro	Trp	Cys 445	Gly	His	Cys
Lys	Asn 450	Leu	Glu	Pro	Lys	Tyr 455	Lys	Glu	Leu	Gly	Glu 460	Lys	Leu	Ser	Lys
Asp 465	Pro	Asn	Ile	Val	Ile 470	Ala	Lys	Met	Asp	Ala 475	Thr	Ala	Asn	Asp	Val 480
Pro	Ser	Pro	Tyr	Glu 485	Val	Arg	Gly	Phe	Pro 490	Thr	Ile	Tyr	Phe	Ser 495	Pro
Ala	Asn	Lys	Lys 500	Leu	Asn	Pro	Lys	Lys 505	Tyr	Glu	Gly	Gly	Arg 510	Glu	Leu

Ser Asp Phe Ile Ser Tyr Leu Gln Arg Glu Ala Thr Asn Pro Pro Val 515 520 525

Ile Gln Glu Lys Pro Lys Lys Lys Lys Ala Gln Glu Asp Leu 530 540

<210> 870

<211> 111

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (17)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 870

Arg Arg Xaa Ala Ile Phe Thr Cys Glu Val Pro Gly Val Tyr Tyr Phe 1 5 10 15

Xaa Tyr His Val His Cys Lys Gly Gly Asn Val Trp Val Ala Leu Phe 20 25 30

Lys Asn Asn Glu Pro Val Met Tyr Thr Tyr Asp Glu Tyr Lys Lys Gly
35 40 45

Phe Leu Asp Gln Ala Ser Gly Ser Ala Val Leu Leu Leu Arg Pro Gly 50 60

Asp Arg Cys Ser Ser Arg Cys Pro Gln Asn Arg Leu Gln Asp Cys Met 65 70 75 80

Pro Gly Ser Met Ser Thr Pro Pro Phe Gln Asp Ile Tyr Cys Ile Pro 85 90 95

Cys Lys Asn Lys Lys Thr Lys Asn Lys Glu Lys Lys Glu Ile Leu 100 105 110

<210> 871 <211> 124

<212> PRT

<213> Homo sapiens

<400> 871

Gly Lys Thr Glu Val Asn Tyr Thr Gln Leu Val Asp Leu His Ala Arg

1 5 10 15

Tyr Ala Glu Cys Gly Leu Arg Ile Leu Ala Phe Pro Cys Asn Gln Phe 20 25 30

Gly Lys Gln Glu Pro Gly Ser Asn Glu Glu Ile Lys Glu Phe Ala Ala 35 40 45

Gly Tyr Asn Val Lys Phe Asp Met Phe Ser Lys Ile Cys Val Asn Gly 50 55 60

Asp Asp Ala His Pro Leu Trp Lys Trp Met Lys Ile Gln Pro Lys Gly 65 70 75 80

Lys Gly Ile Leu Gly Asn Ala Ile Lys Trp Asn Phe Thr Lys Phe Leu $85 \hspace{1cm} 90 \hspace{1cm} 95$

Ile Asp Lys Asn Gly Cys Val Val Lys Arg Tyr Gly Pro Met Glu Glu 100 105 110

Pro Leu Val Ile Glu Lys Asp Leu Pro His Tyr Phe 115 120

<210> 872

<211> 35

<212> PRT

<213> Homo sapiens

<400> 872

Ser Gln His Phe Gly Arg Pro Arg Gln Ala Glu His Leu Lys Glu Phe 1 5 10 15

Lys Thr Ser Val Ala Asn Val Val Asn Pro Val Ser Thr Lys Asn Thr 20 25 30

Lys Ile Val

35

<210> 873

<211> 420

WO 00/55350

	2> Pi 3> Ho	RT omo	sapi	ens											
- 4 0	۸۰ ۸۰	~ ~													
	0> 8: Cys		Gln	Leu 5	Cys	Gln	Ser	Thr	Val 10	Ser	Cys	Pro	Leu	Gly 15	ту
Leu	Ala	Ser	Thr 20	Ala	Thr	Asn	Asp	Cys 25	Gly	Cys	Thr	Thr	Thr 30	Thr	Сys
Leu	Pro	Asp 35	Lys	Val	Суз	Val	His 40	Arg	Ser	Thr	Ile	Туг 45	Pro	Val	Gly
31n	Phe 50	Trp	Glu	Glu	Gly	Cys 55	Asp	Val	Суѕ	Thr	Cys 60	Thr	Asp	Met	G1:
Asp 65	Ala	Val	Met	Gly	Leu 70	Arg	Val	Ala	Gln	Cys 75	Ser	Gln	Lys	Pro	Cys 80
Glu	Asp	Ser	Сув	Arg 85	Ser	Gly	Phe	Thr	Туг 90	Val	Leu	His	Glu	Gly 95	Glu
Cys	Суз	Gly	Arg 100	Суз	Leu	Pro	Ser	Ala 105	Суз	Glu	Val	Val	Thr 110	Gly	Ser
Pro	Arg	Gly 115	Asp	Ser	Gln	Ser	Ser 120	Trp	Lys	Ser	Val	Gly 125	Ser	Gln	Tr
Ala	Ser 130	Pro	Glu	Asn	Pro	Cys 135	Leu	Ile	Asn	Glu	Cys 140	Val	Arg	Val	Lys
31u 145	Glu	Val	Phe	Ile	Gln 150	Gln	Arg	Asn	Val	Ser 155	Cys	Pro	Gln	Leu	Glu 160
/al	Pro	Val	Cys	Pro 165	Ser	Gly	Phe	Gln	Leu 170	Ser	Cys	Lys	Thr	Ser 175	Ala
Cys	Cys	Pro	Ser 180	Cys	Arg	Cys	Glu	Arg 185	Met	Glu	Ala	Cys	Met 190	Leu	Asr
3ly	Thr	Val 195	Ile	Gly	Pro	Gly	Lys 200	Thr	Val	Met	Ile	Asp 205	Val	Cys	Thr
hr	Cys 210	Arg	Cys	Met	Val	Gln 215	Val	Gly	Val	Ile	Ser 220	Gly	Phe	Lys	Leu
31u 225	Cys	Arg	Lys	Thr	Thr 230	Cys	Asn	Pro	Cys	Pro 235	Leu	Gly	Tyr	Lys	Glu 240

Glu Asn Asn Thr Gly Glu Cys Cys Gly Arg Cys Leu Pro Thr Ala Cys

250

255

<220> <221> SITE <222> (103)

Thr Ile Gln Leu Arg Gly Gly Gln Ile Met Thr Leu Lys Arg Asp Glu 265 Thr Leu Gln Asp Gly Cys Asp Thr His Phe Cys Lys Val Asn Glu Arg 280 Gly Glu Tyr Phe Trp Glu Lys Arg Val Thr Gly Cys Pro Pro Phe Asp 290 295 Glu His Lys Cys Leu Ala Glu Gly Gly Lys Ile Met Lys Ile Pro Gly Thr Cys Cys Asp Thr Cys Glu Glu Pro Glu Cys Asn Asp Ile Thr Ala 325 Arg Leu Gln Tyr Val Lys Val Gly Ser Cys Lys Ser Glu Val Glu Val 340 345 Asp Ile His Tyr Cys Gln Gly Lys Cys Ala Ser Lys Ala Met Tyr Ser 360 Ile Asp Ile Asn Asp Val Gln Asp Gln Cys Ser Cys Cys Ser Pro Thr 375 Arg Thr Glu Pro Met Gln Val Ala Leu His Cys Thr Asn Gly Ser Val 390 395 Val Tyr His Glu Val Leu Asn Ala Met Glu Cys Lys Cys Ser Pro Arg 410 Lys Cys Ser Lys 420 <210> 874 <211> 151 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (90)

<223> Xaa equals any of the naturally occurring L-amino acids

<223> Xaa equals any of the naturally occurring L-amino acids

<220> <221> SITE ... <222> (143) <223> Xaa equals any of the naturally occurring L-amino acids <400> 874 Arg Gln Val Pro His Glu Arg Ala Val Arg Asp Gly Arg Gly Gly Arg Ser Arg Gly Ser Lys Leu Thr Tyr Ala Cys Met Arg Arg His Ser Ser Ser Ile Val Ser Pro Lys Phe Asn Ser Leu Ala Val Val Leu Gln Arg Arg Asp Trp Glu Asn Pro Gly Val Thr Gln Leu Asn Arg Leu Ala 50 55 Ala His Pro Pro Phe Ala Ser Trp Arg Asn Ser Glu Glu Ala Arg Thr Asp Ser Pro Phe Pro Asn Ser Cys Ala Xaa Gly Met Ala Asn Gly Asp Ala Pro Cys Met Gly Ala Xaa Lys Arg Gly Gly Cys Gly Gly Tyr Ala 105 Gln Trp Thr Arg Tyr Thr Cys Gln Arg Pro Ser Ala Arg Ser Phe Arg 120 Phe Leu Pro Phe Leu Ser Arg His Val Arg Arg Leu Ser Pro Xaa Ser 135 Ser Lys Ser Val Gly Ser Leu 145 150 <210> 875 <211> 95 <212> PRT <213> Homo sapiens <400> 875 Ala Leu Asn Leu Asn Ser Gln Leu Asn Ile Pro Lys Asp Thr Ser Gln 5

Leu Lys Lys His Ile Thr Leu Leu Cys Asp Arg Leu Ser Lys Gly Gly

Arg Leu Cys Leu Ser Thr Asp Ala Ala Pro Gln Thr Met Val Met

823

35 40 45

Pro Gly Gly Cys Thr Thr Ile Pro Glu Ser Asp Leu Glu Glu Arg Ser
50 60

Val Glu Gln Asp Ser Thr Glu Leu Phe Thr Asn His Arg His Leu Thr 65 70 75 80

Ala Glu Thr Pro Arg Pro Val Ser Pro Leu Gln Gly Val Ser Glu 85 90 95

<210> 876

<211> 238

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (7)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (10)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (15)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (20)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 876

Thr Lys Lys Ala Leu Glu Xaa Ser Asn Xaa Arg Phe Ala Ala Xaa Phe 1 5 10 15

Phe Arg Thr Xaa Trp Asn Pro Pro Gly Ala Phe Lys Glu Phe Gly Thr 20 25 30

Ser Leu Leu Arg Arg Arg Gly Ser Gly Ala Asn Met Pro Val Ala

Arg Ser Trp Val Cys Arg Lys Thr Tyr Val Thr Pro Arg Arg Pro Phe 50 55 60

Glu 65	Lys	Ser	Arg	Leu	Asp 70	Gln	Glu	Leu	Lys	Leu 75	Ile	Gly	Glu	Tyr	G1 ₃
Leu	Arg	Asn	Lys	Arg 85	Glu	Val	Trp	Arg	Val 90	Lys	Phe	Thr	Leu	Ala 95	Ly
Ile	Arg	Lys	Ala 100	Ala	Arg	Glu	Leu	Leu 105	Thr	Leu	Asp	Glu	Lys 110	Asp	Pro
Arg	Arg	Leu 115	Phe	Glu	Gly	Asn	Ala 120	Leu	Leu	Arg	Arg	Leu 125	Val	Arg	Ile
Gly	Val 130	Leu	Asp	Glu	Gly	Lys 135	Met	Lys	Leu	Asp	Tyr 140	Ile	Leu	Gly	Let
Lys 145	Ile	Glu	Asp	Phe	Leu 150	Glu	Arg	Arg	Leu	Gln 155	Thr	Gln	Val	Phe	Lys 160
Leu	Gly	Leu	Ala	Lys 165	Ser	Ile	His	His	Ala 170	Arg	Val	Leu	Ile	Arg 175	Glr
Arg	His	Ile	Arg 180	Val	Arg	Lys	Gln	Val 185	Val	Asn	Ile	Pro	Ser 190	Phe	Ile
Val	Arg	Leu 195	Asp	Ser	Gln	Lys	His 200	Ile	Asp	Phe	Ser	Leu 205	Arg	Ser	Pro
Tyr	Gly 210	Gly	Gly	Arg	Pro	Gly 215	Arg	Val	Lys	Arg	Lys 220	Asn	Ala	Lys	Lys
Gly 225	Gln	Gly	Gly	Ala	Gly 230	Ala	Gly	Asp	Asp	Glu 235	Glu	Glu	Asp		

<210> 877

<211> 79

<212> PRT

<213> Homo sapiens

<400> 877

Ala Gly Ile Arg His Glu Pro Ser Ala Ala Ala Met Ser Ser Gly Ala 1 5 10 15

Ser Ala Ser Ala Leu Gln Arg Leu Val Glu Gln Leu Lys Leu Glu Ala 20 25 30

Gly Val Glu Arg Ile Lys Val Ser Gln Ala Ala Ala Glu Leu Gln Gln 35 40 45

Tyr Cys Met Gln Asn Ala Cys Lys Asp Ala Leu Leu Val Gly Val Pro

WO 00/55350

825

50 55 60

Ala Gly Ser Asn Pro Phe Arg Glu Pro Arg Ser Cys Ala Leu Leu 65 70 75

<210> 878

<211> 136

<212> PRT

<213> Homo sapiens

<400> 878

Ile Ala Ile Met Asn Asp Thr Val Thr Ile Arg Thr Arg Lys Phe Met

1 10 15

Thr Asn Arg Leu Cln Arg Lys Gln Met Val Ile Asp Val Leu His
20 25 30

Pro Gly Lys Ala Thr Val Pro Lys Thr Glu Ile Arg Glu Lys Leu Ala 35 40 45

Lys Met Tyr Lys Thr Thr Pro Asp Val Ile Phe Val Phe Gly Phe Arg 50 $$ \phantom

Thr His Phe Gly Gly Gly Lys Thr Thr Gly Phe Gly Met Ile Tyr Asp
65 70 75 80

Ser Leu Asp Tyr Ala Lys Lys Asn Glu Pro Lys His Arg Leu Ala Arg 85 90 95

His Gly Leu Tyr Glu Lys Lys Lys Thr Ser Arg Lys Gln Arg Lys Glu 100 105 110

Arg Lys Asn Arg Met Lys Lys Val Arg Gly Thr Ala Lys Ala Asn Val 115 120 125

Gly Ala Gly Lys Lys Pro Lys Glu 130 135

<210> 879

<211> 141

<212> PRT

<213> Homo sapiens

<400> 879

Gly Cys Val Gly Val Arg Pro Ser Leu His Pro Ala Thr Ser Thr Ala
1 5 10 15

Ser Gly Ser Ala Ser Pro Thr Leu Ala Arg Ala Met Ala Ser Val Ser 20 25 Glu Leu Ala Cys Ile Tyr Ser Ala Leu Ile Leu His Asp Asp Glu Val 40 Thr Val Thr Glu Asp Lys Ile Asn Ala Leu Ile Lys Ala Ala Gly Val Asn Val Glu Pro Phe Trp Pro Gly Leu Phe Ala Lys Ala Leu Ala Asn 70 Val Asn Ile Gly Ser Leu Ile Cys Asn Val Gly Ala Gly Gly Pro Ala Pro Ala Ala Gly Ala Ala Pro Ala Gly Gly Pro Ala Pro Ser Thr Ala 105 Ala Ala Pro Ala Glu Glu Lys Lys Val Glu Ala Lys Lys Glu Glu Ser 115 120 Glu Glu Ser Asp Asp Met Gly Phe Gly Leu Phe Asp 135 <210> 880 <211> 133 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (14) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (19) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (128) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (130)

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<221> SITE <222> (136) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (171) <223> Xaa equals any of the naturally occurring L-amino acids <400> 881 Ile Glu Glu Pro Arg Asp Thr Arg Leu Gln Val Cys Ser Xaa Val His Ile Trp Cys Leu Asp Lys Phe Lys Met Arg Lys His Arg His Leu Pro 20 25 Leu Val Ala Val Phe Cys Leu Phe Leu Ser Gly Phe Pro Thr Thr His Ala Gln Gln Gln Ala Val Ile Glu Val Asn Lys Arg Asp Ile Val 55 Phe Leu Val Asp Gly Ser Ser Ala Leu Gly Leu Ala Asn Phe Asn Ala 70 Ile Arg Asp Phe Ile Ala Lys Val Ile Gln Arg Leu Glu Ile Gly Gln Asp Leu Ile Gln Val Ala Val Ala Gln Tyr Ala Asp Thr Val Arg Pro 105 Glu Phe Tyr Phe Asn Thr His Pro Thr Lys Arg Xaa Val Ile Thr Ala 115 120 Val Arg Lys Met Lys Pro Leu Xaa Gly Ser Ala Leu Tyr Thr Gly Ser 135 , Ala Leu Asp Phe Val Arg Asn Asn Leu Phe Thr Ser Ser Ala Gly Tyr 145 150 155 160 Arg Ala Ala Glu Gly Ile Pro Lys Leu Leu Xaa Leu Ile Thr Gly Gly 165 170 Lys Ser Leu Asp Glu Ile Ser Gln Pro Ala Gln Glu Leu Lys Arg Ser 185 Ser Ile Met Ala Phe Ala Ile Gly Asn Lys Gly Ala Asp Gln Ala Glu 195

Leu Glu Glu Ile Ala Phe Asp Ser Ser Leu Val Phe Ile Pro Ala Glu

220

215

Phe Arg Ala Ala Pro Leu Gln Gly Met Leu Pro Gly Leu Leu Ala Pro 225 230 235 Leu Arg Thr Leu Ser Gly Thr Pro Glu Val His Ser Asn Lys Arg Asp 245 250 Ile Ile Phe Leu 260 <210> 882 <211> 149 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (1) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (2) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (6) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (9) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (13) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (16) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (19) <223> Xaa equals any of the naturally occurring L-amino acids

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Xaa Xaa Glu Ser Glu Xaa Ser Phe Xaa Cys Arg Lys Xaa Ile Ile Xaa 1 5 10 15

Phe Leu Xaa Tyr Lys Arg Val Val Phe Leu Lys Gln Leu Ala Ser Gly 20 25 30

Leu Leu Val Thr Gly Pro Leu Val Leu Asn Arg Val Pro Leu Arg
35 . 40 45

Arg Thr His Gln Lys Phe Val Ile Ala Thr Ser Thr Lys Ile Asp Ile
50 55 60

Ser Asn Val Lys Ile Pro Lys His Leu Thr Asp Ala Tyr Phe Lys Lys 65 70 75 80

Lys Lys Leu Arg Lys Pro Arg His Gln Glu Gly Glu Ile Phe Asp Thr 85 90 95

Glu Lys Glu Lys Tyr Glu Ile Thr Glu Gln Arg Lys Ile Asp Gln Lys 100 105 110

Ala Val Asp Ser Gln Ile Leu Pro Lys Ile Lys Ala Ile Pro Gln Leu 115 120 125

Gln Gly Tyr Leu Arg Ser Val Phe Ala Leu Thr Asn Gly Ile Tyr Pro 130 135 140

His Lys Leu Val Phe 145

<210> 883

<211> 256

<212> PRT

<213> Homo sapiens

<400> 883

Trp Lys Ser Val Val Val Leu Ala Val Ser Ala Gly Ala Gly Ser Ala 1 5 10 15

His Pro Arg Gln Asn Lys Tyr Ser Val Leu Leu Pro Thr Tyr Asn Glu 20 25 30

Arg Glu Asn Leu Pro Leu Ile Val Trp Leu Leu Val Lys Ser Phe Ser 35 40 45

Glu Ser Gly Ile Asn Tyr Glu Ile Ile Ile Ile Asp Asp Gly Ser Pro
50 60

Asp 65	Gly	Thr	Arg	Asp	Val 70	Ala	Glu	Gln	Leu	Glu 75	Lys	Ile	Tyr	Gly	Ser 80
Asp	Arg	Ile	Leu	Leu 85	Arg	Pro	Arg	Glu	Lys 90	Lys	Leu	Gly	Leu	Gly 95	Thr
Ala	Tyr	Ile	His 100	Gly	Met	Lys	His	Ala 105	Thr	Gly	Asn	Tyr	Ile 110	Ile	Ile
Met	Asp	Ala 115	Asp	Leu	Ser	His	His 120	Pro	Lys	Phe	Ile	Pro 125	Glu	Phe	Ile
Arg	Lys 130	Gln	Lys	Glu	Gly	Asn 135	Phe	Asp	Ile	Val	Ser 140	Gly	Thr	Arg	Tyr
Lys 145	Gly	Asn	Gly	Gly	Val 150	Tyr	Gly	Trp	Asp	Leu 155	Lys	Arg	Lys	Ile	Ile 160
Ser	Arg	Gly	Ala	Asn 165	Phe	Leu	Thr	Gln	Ile 170	Leu	Leu	Arg	Pro	Gly 175	Ala
Ser	Asp	Leu	Thr 180	Gly	Ser	Phe	Arg	Leu 185	Туг	Arg	Lys	Glu	Val 190	Leu	Glu
Lys	Leu	Ile 195	Glu	Lys	Cys	Val	Ser 200	Lys	Gly	Tyr	Val	Phe 205	Gln	Met	Glu
Met	Ile 210	Val	Arg	Ala	Arg	Gln 215	Leu	Asn	Tyr	Thr	Ile 220	Gly	Glu	Val	Pro
11e 225	Ser	Phe	Val	Asp	Arg 230	Val	Tyr	Gly	Glu	Ser 235	Lys	Leu	Gly	Gly	Asn 240
Glu	Ile	Val	Ser	Phe 245	Leu	Ĺys	Gly	Leu	Leu 250	Thr	Leu	Phe	Ala	Thr 255	Thr

<210> 884

<211> 449

<212> PRT

<213> Homo sapiens

<400> 884

Gly Gly Ser Trp Cys Arg Ser Ser Pro Gly Arg Asp Gly Ser Pro Gly 1 5 15

Ala	Lys	Gly	Asp 20	Arg	Gly	Glu	Thr	Gly 25	Pro	Ala	Gly	Pro	Pro 30	Gly	Ala
Pro	Gly	Ala 35	Pro	Gly	Ala	Pro	Gly 40	Pro	Val	Gly	Pro	Ala 45	Gly	Lys	Ser
Gly	Asp 50	Arg	Gly	Glú	Thr	Gly 55	Pro	Ala	Gly	Pro	Ala 60	Gly	Pro	Val	Gly
Pro 65	Val	Gly	Ala	Arg	Gly 70	Pro	Ala	Gly	Pro	Gln 75	Gly	Pro	Arg	Gly	Asp 80
Lys	Gly	Glu	Thr	Gly 85	Glu	Gln	Gly	Asp	Arg 90	Gly	Ile	Ļys	Gly	His 95	Arg
Gly	Phe	Ser	Gly 100	Leu	Gln	Gly	Pro	Pro 105	Gly	Pro	Pro	Gly	Ser 110	Pro	Gly
Glu	Gln	Gly 115	Pro	Ser	Gly	Ala	Ser 120	Gly	Pro	Ala	Gly	Pro 125	Arg	Gly	Pro
Pro	Gly 130	Ser	Ala	Gly	Ala	Pro 135	Gly	Lys	Asp	Gly	Leu 140	Asn	Gly	Leu	Pro
Gly 145	Pro	Ile	Gly	Pro	Pro 150	Gly	Pro	Arg	Gly	Arg 155	Thr	Gly	Asp	Ala	Gly 160
Pro	Val	Gly	Pro	Pro 165	Gly	Pro	Pro	Gly	Pro 170	Pro	Gly	Pro	Pro	Gly 175	Pro
Pro	Ser	Ala	Gly 180	Phe	Asp	Phe	Ser	Phe 185	Leu	Pro	Gln	Pro	Pro 190	Gln	Glu
Lys	Ala	His 195	Asp	Gly	Gly	Arg	Tyr 200	Tyr	Arg	Ala	Asp	Asp 205	Ala	Asn	Val
Val	Arg 210	Asp	Arg	Asp	Leu	Glu 215	Val	Asp	Thr	Thr	Leu 220	Lys	Ser	Leu	Ser
Gln 225	Gln	Ile	Glu	Asn	Ile 230	Arg	Ser	Pro	Glu	Gly 235	Ser	Arg	Lys	Asn	Pro 240
Ala	Arg	Thr	Cys	Arg 245	Asp	Leu	Lys	Met	Cys 250	His	Ser	Asp	Trp	Lys 255	Ser
Gly	Glu	Tyr	Ţrp 260	Ile	Asp	Pro	Asn	Gln 265	Gly	Cys	Asn	Leu	Asp 270	Ala	Ile
Lys	Val	Phe	Cys	Asn	Met		Thr	Gly	Glu	Thr	Cys	Val	Tyr	Pro	Thr

Gln Pro Ser Val Ala Gln Lys Asn Trp Tyr Ile Ser Lys Asn Pro Lys 295

Asp Lys Arg His Val Trp Phe Gly Glu Ser Met Thr Asp Gly Phe Gln 310 315

Phe Glu Tyr Gly Gly Gln Gly Ser Asp Pro Ala Asp Val Ala Ile Gln 330

Leu Thr Phe Leu Arg Leu Met Ser Thr Glu Ala Ser Gln Asn Ile Thr 350 340 345

Tyr His Cys Lys Asn Ser Val Ala Tyr Met Asp Gln Gln Thr Gly Asn 360

Leu Lys Lys Ala Leu Leu Gln Gly Ser Asn Glu Ile Glu Ile Arg 375

Ala Glu Gly Asn Ser Arg Phe Thr Tyr Ser Val Thr Val Asp Gly Cys 395 385 390

Thr Ser His Thr Gly Ala Trp Gly Lys Thr Val Ile Glu Tyr Lys Thr 405 410

Thr Lys Thr Ser Arg Leu Pro Ile Ile Asp Val Ala Pro Leu Asp Val 425

Gly Ala Pro Asp Gln Glu Phe Gly Phe Asp Val Gly Pro Val Cys Phe 440 435

Leu

<210> 885

<211> 64

<212> PRT

<213> Homo sapiens

<400> 885

Gly Lys Leu Val Thr Leu Gln Val Pro Val Arg Asn Ser Arg Val Asp 10

Pro Arg Val Arg Trp Gly Phe Thr Lys Phe Asn Ala Asp Glu Phe Glu

Âsp Met Val Ala Glu Lys Arg Leu Ile Pro Asp Gly Cys Gly Val Lys ` 40

Tyr Ile Pro Ser Arg Gly Pro Leu Asp Lys Trp Arg Ala Leu His Ser

WO 00/55350 PCT/US00/05882

834

50 55 . 60

<210> 886

<211> 132

<212> PRT

<213> Homo sapiens

<400> 886

Thr Thr Leu Arg Ala Leu Ala Leu Asn Leu Trp Pro Pro Lys Ser Arg
1 5 10 15

Ser Leu Ile Ser Ser Trp Gln Ser Cys Gly Gln Glu Val Leu Lys Gly
20 25 30

Lys Thr His Ser Asp Asn Cys Ser Pro Ile Tyr Gln Pro Ser Ala Gly 35 40

Val Ser Asp Arg Gly Pro Leu Pro Pro Leu Glu Cys Ala Thr Tyr Glu 50 55 60

Glu Cys Pro Met Gly Lys Arg Arg Leu Ser Cys Pro Leu Ala Ala Cys
65 70 75 . 80

Ala Ser Ile Pro Gly Gln Lys Phe Pro Gln Glu Pro Leu Ala Leu Ala 85 90 95

Gln Ser His Cys Glu Arg Arg Trp Glu Pro Thr Pro Leu Gly Glu Gly 100 105 110

Ala Val Leu Leu Gly Thr Ser Gln His Gln Val Arg Ser Leu Lys Leu 115 120 125

Lys Asn Val Asn 130

<210> 887

<211> 70

<212> PRT

<213> Homo sapiens

<400> 887

Gly Leu Ser Ser Glu Ala Arg Glu Lys Ser Ser Glu Pro Gln Glu Arg

1 5 10 15

Ser Ser Glu Pro Trp Glu Arg Ser Ser Glu Pro Trp Glu Gly Leu Val Thr Phe Glu Asp Val Ala Val Glu Phe Thr Gln Glu Glu Trp Ala Leu Leu Asp Pro Ala Gln Arg Thr Leu Tyr Arg Asp Val Met Leu Glu Asn 55 Cys Arg Thr Trp Pro His 65 <210> 888 <211> 373 <212> PRT <213> Homo sapiens <400> 888 Val Asp Pro Arg Val Arg Phe Arg Glu Glu Phe Leu Phe Ser Ser Leu Gln Glu Gly Arg Asp Lys Asp Thr Phe Ser Lys Met Ala Met Val Ser 25 Glu Phe Leu Lys Gln Ala Trp Phe Ile Glu Asn Glu Glu Gln Glu Tyr 40 Val Gln Thr Val Lys Ser Ser Lys Gly Gly Pro Gly Ser Ala Val Ser 55 Pro Tyr Pro Thr Phe Asn Pro Ser Ser Asp Val Ala Ala Leu His Lys 70 75 Ala Ile Met Val Lys Gly Val Asp Glu Ala Thr Ile Ile Asp Ile Leu 85 Thr Lys Arg Asn Asn Ala Gln Arg Gln Gln Ile Lys Ala Ala Tyr Leu 100 Gln Glu Thr Gly Lys Pro Leu Asp Glu Thr Leu Lys Lys Ala Leu Thr 120

Gly His Leu Glu Glu Val Val Leu Ala Leu Leu Lys Thr Pro Ala Gln

Phe Asp Ala Asp Glu Leu Arg Ala Ala Met Lys Gly Leu Gly Thr Asp

Glu Asp Thr Leu Ile Glu Ile Leu Ala Ser Arg Thr Asn Lys Glu Ile

135

170 165 175 Arg Asp Ile Asn Arg Val Tyr Arg Glu Glu Leu Lys Arg Asp Leu Ala Lys Asp Ile Thr Ser Asp Thr Ser Gly Asp Phe Arg Asn Ala Leu Leu Ser Leu Ala Lys Gly Asp Arg Ser Glu Asp Phe Gly Val Asn Glu Asp 215 Leu Ala Asp Ser Asp Ala Arg Ala Leu Tyr Glu Ala Gly Glu Arg Arg 230 Lys Gly Thr Asp Val Asn Val Phe Asn Thr Ile Leu Thr Thr Arg Ser Tyr Pro Gln Leu Arg Arg Val Phe Gln Lys Tyr Thr Lys Tyr Ser Lys . 265 His Asp Met Asn Lys Val Leu Asp Leu Glu Leu Lys Gly Asp Ile Glu Lys Cys Leu Thr Ala Ile Val Lys Cys Ala Thr Ser Lys Pro Ala Phe 295 Phe Ala Glu Lys Leu His Gln Ala Met Lys Gly Val Gly Thr Arg His 305 Lys Ala Leu Ile Arg Ile Met Val Ser Arg Ser Glu Ile Asp Met Asn Asp Ile Lys Ala Phe Tyr Gln Lys Met Tyr Gly Ile Ser Leu Cys Gln 345 Ala Ile Leu Asp Glu Thr Lys Gly Asp Tyr Glu Lys Ile Leu Val Ala 360 Leu Cys Gly Gly Asn

<210> 889

370

<211> 336

<212> PRT

<213> Homo sapiens

<220>

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<222> (7)

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<222> (183)
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<400> 889
Gly Arg Lys Lys His Leu Xaa Ala Arg Leu Val Thr Glu Met Asp Ser
Lys Tyr Gln Cys Val Lys Leu Asn Asp Gly His Phe Met Pro Val Leu
             20
Gly Phe Gly Thr Tyr Ala Pro Ala Glu Val Pro Lys Ser Lys Ala Leu
Glu Ala Xaa Lys Leu Ala Ile Glu Ala Gly Phe Xaa His Ile Asp Ser
     50
                         55
Ala His Xaa Tyr Asn Asn Glu Glu Gln Val Gly Leu Ala Ile Arg Ser
 65
                     70
Lys Ile Ala Asp'Gly Ser Val Lys Arg Glu Asp Ile Phe Tyr Thr Ser
Lys Leu Trp Xaa Asn Ser His Arg Pro Glu Leu Val Arg Pro Ala Leu
            100
Glu Arg Ser Leu Lys Asn Leu Gln Leu Asp Tyr Val Asp Leu Tyr Leu
                            120
        115
                                                125
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Ile	His 130	Phe	Pro	Val	Ser	Val 135	Lys	Pro	Gly	Glu	Glu 140	Val	Ile	Pro	Lys
Asp 145	Glu	Asn	Gly	Lys	Ile 150	Leu	Phe	Asp	Thr	Val 155	Asp	Leu	Cys	Ala	Thr 160
Trp	Glu	Ala	Val	Glu 165	Lys	Cys	Lys	Asp	Ala 170	Gly	Leu	Ala	Lys	Ser 175	Ile
Gly	Val	Ser	Asn 180	Phe	Asn	Xaa	Arg	Gln 185	Leu	Glu	Met	Ile	Leu 190	Asn	Lys
Pro	Gly	Leu 195	Lys	Tyr	Lys	Pro	Val 200	Сув	Asn	Gln	Val	Glu 205	Суs	His	Pro
Tyr	Phe 210	Asn	Gln	Arg	Lys	Leu 215	Leu	Asp	Phe	Cys	Lys 220	Ser	Lys	Asp	Ile
Val 225	Leu	Val	Ala	Tyr	Ser 230	Ala	Leu	Gly	Ser	His 235	Arg	Glu	Glu	Pro	Trp 240
Val	Asp	Pro	Asn	Ser 245	Pro	Val	Leu	Leu	Glu 250	Asp	Pro	Val	Leu	Cys 255	Ala
Leu	Ala	Lys	Lys 260	His	Lys	Arg	Thr	Pro 265	Ala	Leu	Ile	Ala	Leu 270	Arg	Tyr
Gln	Leu	Gln 275	Arg	Gly	Val	Val	Val 280	Leu	Ala	Lys	Ser	Туг 285	Asn	Glu	Gln
Arg	Ile 290	Arg	Gln	Asn	Val	Gln 295	Val	Phe	Glu	Phe	Gln 300	Leu	Thr	Ser	Glu
Glu 305	Met	Lys	Ala	Ile	Asp 310	Gly	Leu	Asn	Arg	Asn 315	Val	Arg	Tyr	Leu	Thr 320
Leu	Asp	Ile	Phe	Ala 325	Gly	Pro	Pro	Asn	Tyr 330	Pro	Phe	Ser	Asp	Glu 335	туг

<210> 890

<211> 195

<212> PRT

<213> Homo sapiens

<400> 890

PCT/US00/05882

Arg Ser Ser Glu Val Tyr Ala Gln Leu Cys Asn Val Ala Arg Ile Glu
1 5 10 15

Ala Glu Arg Glu Ala Gly Val His Phe Arg Pro Gly Tyr Glu Tyr Gly
20 25 30

Pro Gly Pro Asp Asp Leu His Tyr Ser Ile Tyr Gly Pro Asp Gly Ala 35 40 45

Pro Phe Tyr Asn Tyr Leu Gly Pro Glu Asp Thr Val Pro Glu Pro Ala 50 55 60

Phe Pro Asn Thr Ala Gly His Ser Ala Asp Arg Thr Pro Ile Leu Glu 65 70 75 80

Ser Pro Leu Gln Pro Ser Glu Leu Gln Pro His Tyr Val Ala Ser His 85 90 95

Pro Glu Pro Pro Ala Gly Phe Glu Gly Leu Gln Ala Glu Glu Cys Gly
100 105 110

Ile Leu Asn Gly Cys Glu Asn Gly Arg Cys Val Arg Val Arg Glu Gly
115 120 125

Tyr Thr Cys Asp Cys Phe Glu Gly Phe Gln Leu Asp Ala Ala His Met 130 135 140

Leu Cys Val His Gly Tyr Cys Glu Asn Thr Glu Gly Ser Tyr Arg Cys 165 170 175

His Cys Ser Pro Gly Tyr Val Ala Glu Ala Gly Pro Pro His Cys Thr 180 185 190

Ala Lys Glu 195

<210> 891

<211> 198

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (108)

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			-		-				_		Ī				
<40	0> 8	91													
			T.em	Thr	Ġlw	Ara	Tle	Δla	Pho	Δ1 a	Δla	Δla	Arg	Pro	G1 r
	ALG	GLy	Dea	5	GLY	nry	110	niu	10	nia	n. u	. nru	nr 9	15	U
1				3				,	10					13	
•	•		_		_	_					_				
Thr	Pne	Val		GTÄ	Pro	ser	ser		Pro	Pro	Pro	Pro	Pro	PIO	Arç
			20					25					30		
Pro	Ala	Glu	Leu	Ala	Pro	Ser	Pro	Pro	Ala	Asp	Met	Ser	Glu	Ser	Lys
		35					40					45			
Ser	Gly	Pro	Glu	Tyr	Ala	Ser	Phe	Phe	Ala	Val	Met	Gly	Ala	Ser	Ala
	50			_		55					60				
Ala	Met	Val	Phe	Ser	Ala	Leu	Glv	Ala	Ala	Tvr	Glv	Thr	Ala	Lvs	Ser
65					70		1			75	1			-1-	80
0.5					, ,					, ,					•
C1	. mh ~	C1.	T10	21-	712	Mot	50×	17 n 1	Mot	۸۳۵	Dro	C1	Cln.	Tla	Mat
GIY	THE	GIY	TIE		HIG	met	ser	val		Arg	PIO	GIU	Gln		met
				85					90					95	
_	_		·	_				_ •						_	
Lys	Ser	Ile		Pro	Val	Val	Met		Gly	He	Xaa	Xaa	Ile	Tyr	Gly
			100					105					110		
Leu	Val	Val	Ala	Val	Leu	Ile	Ala	Asn	Ser	Leu	Asn	Asp	Asp	Ile	Ser
		115					120					125			
Leu	Tyr	Lys	Ser	Phe	Leu	Gln	Leu	Gly	Ala	Gly	Leu	Ser	Val	Gly	Leu
	130	_				135				-	140			_	
					,										
Ser	Glv	Leu	Ala	Ala	Glv	Phe	Ala	Ile	Glv	Ile	Val	Glv	Asp	Ala	Glv
145	1				150				2	155		3			160
143					130										100
17-1	N	C1	7.00	77.	C1 -	C1 -	D=-	n ~ ~	T 011	Dho	17.1	c1	Met	T1.	T
Val	ALG	GLY	ASII		GIII	GIII	FIO	ALG		FIIC	Val	GLY	Met		nea
				165					170					175	
									_			_			_
Ile	Leu	Ile		Ala	Glu	Val	Leu	_	Leu	Tyr	Gly	Leu	Ile	Val	Ala
			180		•			185					190		

<210> 892

<211> 95

<212> PRT

<213> Homo sapiens

195

Leu Ile Leu Ser Thr Lys

<400> 892 Asp Ala Trp Ala Pro Ser Glu Ser Arg Glu Ala Leu Leu Thr Pro Pro Pro His Arg Arg His Thr Ala Ala Ala Ser Val Met Pro Lys His Glu 20 25 Phe Ser Val Asp Met Thr Cys Gly Gly Cys Ala Glu Ala Val Ser Arg Val Leu Asn Lys Leu Gly Gly Val Lys Tyr Asp Ile Asp Leu Pro Asn 50 55 Lys Lys Val Cys Ile Glu Ser Glu His Ser Met Asp Thr Leu Leu Ala 70 Thr Leu Lys Lys Thr Gly Lys Thr Val Ser Tyr Leu Gly Leu Glu 90 <210> 893 <211> 123 . <212> PRT <213> Homo sapiens <220> <221> SITE <222> (111) <223> Xaa equals any of the naturally occurring L-amino acids

<221> SITE

<220>

<222> (117)

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<400> 893

Gly Glu His Pro Arg Gln Pro Ala Gly Asn Asn Ile Leu Ala Val Leu 1 5 10 15

Thr Cys Cys Gln Gln Ile His Arg Thr Trp Met Lys Phe Pro Phe Pro 20 25 30

Leu Val Ser Ser Cys Ser Thr Pro Leu Leu Asp Pro Lys Ser Leu Thr 35 40 45

Lys Ala Leu Asn Thr Val Lys Met Phe Tyr Ile Pro Phe His Leu Cys
50 55 60

Cys Phe Phe Asn Cys Ile Leu Pro Asp Val Leu Met Leu Ser Leu Met

65 70 75 Leu Ile Val Ile Pro Val Arg Val His Phe Ile Phe Met Leu Phe Gln 85 90 Pro Cys Ile Asn Ile His Leu Thr Lys Ile Thr Gln Leu Ile Xaa Lys Lys Lys Lys Asn Xaa Gly Gly Gly Pro Gly Thr <210> 894 <211> 172 <212> PRT <213> Homo sapiens <400> 894 Gln Phe Val Tyr Cys Gly Lys Lys Ala Gln Leu Asn Ile Gly Asn Val 10 Leu Pro Val Gly Thr Met Pro Glu Gly Thr Ile Val Cys Cys Leu Glu 20 25 Glu Lys Pro Gly Asp Arg Gly Lys Leu Ala Arg Ala Ser Gly Asn Tyr 40 Ala Thr Val Ile Ser His Asn Pro Glu Thr Lys Lys Thr Arg Val Lys Leu Pro Ser Gly Ser Lys Lys Val Ile Ser Ser Ala Asn Arg Ala Val 65 70 Val Gly Val Val Ala Gly Gly Gly Arg Ile Asp Lys Pro Ile Leu Lys Ala Gly Arg Ala Tyr His Lys Tyr Lys Ala Lys Arg Asn Cys Trp Pro 100 105 110 Arg Val Arg Gly Val Ala Met Asn Pro Val Glu His Pro Phe Gly Gly 120 Gly Asn His Gln His Ile Gly Lys Pro Ser Thr Ile Arg Arg Asp Ala 135 Pro Ala Gly Arg Lys Val Gly Leu Ile Ala Ala Arg Arg Thr Gly Arg 145 155

Leu Arg Gly Thr Lys Thr Val Gln Glu Lys Glu Asn

170

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<210> 897

<211> 289

<212> PRT

<213> Homo sapiens

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<400> 897

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Arg Val Arg Gly Arg Ser Gln Leu Ser Ala His Gly Pro Ala Ser Phe 20 25 30

Lys Met Ser Thr Val His Glu Ile Leu Cys Lys Leu Ser Leu Glu Gly
35 40 45

Asp	His 50	Ser	Thr	Pro	Pro	Ser 55	Ala	Tyr	Gly	Ser	Val 60	Lys	Ala	Tyr	Thr
Asn 65	Phe	Asp	Ala	Glu	Arg 70	Asp	Ala	Leu	Asn	Ile 75	Glu	Thr	Ala	Ile	Lys 80
Thr	Lys	Gly	Val	Asp 85	Glu	Val	Thr	Ile	Val 90	Asn	Ile	Leu	Thr	Asn 95	Arg
Ser	Asn	Ala	Gln 100	Arg	Gln	Asp	Ile	Ala 105	Phe	Ala	Tyr	Gln	Arg 110	Arg	Thr
Lys	Lys	Glu 115	Leu	Ala	Ser	Ala	Leu 120	Lys	Ser	Ala	Leu	Ser 125	Gly	His	Leu
Glu	Thr 130	Val	Ile	Leu	Gly	Leu 135	Leu	Lys	Thr	Pro	Ala 140	Gln	Tyr	Asp	Ala
Ser 145	Glu	Leu	Lys	Ala	ser 150	Met	Lys	Gly	Leu	Gly 155	Thr	Asp	Glu	Asp	Ser 160
Leu	Ile	Glu	Ile	Ile 165	Cys	Ser	Arg	Thr	Asn 170	Gln	Glu	Leu	Gln	Glu 175	Ile
Asn	Arg	Val	Туг 180	Lys	Glu	Met	Tyr	Lys 185	Thr	Asp	Leu	Glu	Lys 190	Asp	Ile
Ile	Ser	Asp 195	Thr	Ser	Gly	Asp	Phe 200	Arg	Lys	Leu	Met	Val 205		Leu	Ala
Lys	Gly 210	Arg	Arg	Ala	Glu	Asp 215	Gly	Ser	Val	Ile	Asp 220	Tyr	Glu	Leu	Ile
Asp 225	Gln	Asp	Ala	Arg	Asp 230	Leu	туr	Asp	Ala	Gly 235	Val	Lys	Arg	Lys	Gly 240
Thr	Asp	Val	Pro	Lys 245	Trp	Ile	Ser	Ile	Met 250	Thr	Glu	Arg	Ser	Xaa 255	Pro
Thr	Ser	Arg	Lys 260	Tyr	Leu	Ile	Gly	Thr 265	Arg	Val	Thr	Ala	Leu 270	Met	Thr
Cys	Trp	Lys 275	Ala	Ser	Gly	Lys	Arg 280	Leu	Lys	Glu	Thr	Trp 285	Lys	Met	Leu

Ser

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		omo	sapi	ens											
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	0> 8								_	_	_			_	
Asn 1	Pro	Arg	Gly	Lys 5	Val	Ala	Gly	Phe	Asp 10	Leu	Asp	GIÀ	Thr	Leu 15	Ile
Thr	Thr	Arg	Ser 20	Gly	Lys	Val	Phe	Pro 25	Thr	Gly	Pro	Ser	Asp 30	Trp	Arg
Ile	Leu	Tyr 35	Pro	Glu	Ile	Pro	Arg 40	Lys	Leu	Arg	Glu	Leu 45	Glu	Ala	Glu
Gly	Tyr 50	Lys	Leu	Val	Ile	Phe 55	Thr	Asn	Gln	Met	Ser 60	Ile	Gly	Arg	Gly
Lys 65	Leu	Pro	Ala	Glu	Glu 70	Phe	Lys	Ala	Lys	Val 75	Glu	Ala	Val	Val	Glu 80
Lys	Leu	Gly	Val	Pro 85	Phe	Gln	Val	Leu	Val 90	Ala	Thr	His	Ala	Gly 95	Leu
Туг	Arg	Lys	Pro 100	Val	Thr	Gly	Met	Trp 105	Asp	His	Leu	Gln	Glu 110	Gln	Ala
Asn	Asp	Gly 115	Thr	Pro	Ile	Ser	Ile 120	Gly	Asp	Ser	Ile	Phe 125	Val	Gly	Asp
Ala	Ala 130	Gly	Arg	Pro	Ala	Asn 135	Trp	Ala	Pro	Gly	Arg 140	Lys	Lys	Lys	Asp
Phe 145	Ser	Суѕ	Ala	Asp	Arg 150	Leu	Phe	Ala	Leu	Asn 155	Leu	Gly	Leu	Pro	Phe 160
Ala	Thr	Pro	Glu	Glu 165	Phe	Phe	Leu	Lys	Trp 170	Pro	Ala	Ala	Gly	Phe 175	Glu
Leu	Pro	Ala	Phe 180	Asp	Pro	Arg	Thr	Val 185	Ser	Arg	Ser	Gly	Pro 190	Leu	Cys
Leu	Pro	Glu 195	Ser	Arg	Ala	Leu	Leu 200	Ser	Ala	Thr	Arg	Xaa 205	Trp	Leu	Ser
Gln	Trp	Asp	Ser	Leu	Gly	Pro	Gly	Ser	Pro	Pro	Phe	Ser	Arg	Ser	Thr

WO 00/55350 PCT/US00/05882

847

210 215 220

Ser Cys Arg Pro Asp Met Ser Thr 225 230

<210> 899

<211> 218

<212> PRT

<213> Homo sapiens

<400> 899

Leu Arg Val Ala Arg Pro Asp Ala Ala Arg Ala Ala Pro Leu Ala Pro 1 5 10 15

Ala Ala Met Lys Ala Val Val Gln Arg Val Thr Arg Ala Ser Val
20 25 30

Thr Val Gly Glu Glu Ile Ser Ala Ile Gly Arg Gly Ile Cys Val

Leu Leu Gly Ile Ser Leu Glu Asp Thr Gln Lys Glu Leu Glu His Met 50 55

Val Arg Lys Ile Leu Asn Leu Arg Val Phe Glu Asp Glu Ser Gly Lys
65 70 75 80

His Trp Ser Lys Ser Val Met Asp Lys Gln Tyr Glu Ile Leu Cys Val 85 90 95

Ser Gln Phe Thr Leu Gln Cys Val Leu Lys Gly Asn Lys Pro Asp Phe 100 105 110

His Leu Ala Met Pro Thr Glu Gln Ala Glu Gly Phe Tyr Asn Ser Phe 115 120 125

Leu Glu Gln Leu Arg Lys Thr Tyr Arg Pro Glu Leu Ile Lys Asp Gly
130 135 140

Lys Phe Gly Ala Tyr Met Gln Val His Ile Gln Asn Asp Gly Pro Val 145 150 155 160

Thr Ile Glu Leu Glu Ser Pro Ala Pro Gly Thr Ala Thr Ser Asp Pro 165 170 175

Lys Gln Leu Ser Lys Leu Glu Lys Gln Gln Arg Lys Glu Lys Thr 180 185 190

Arg Ala Lys Gly Pro Ser Glu Phe Lys Gln Gly Lys Lys His Ser Pro 195 200 205

Lys Arg Arg Pro Gln Cys Gln Gln Arg Gly 210 215

<210> 900

<211> 152

<212> PRT

<213> Homo sapiens

<400> 900

Ser Lys Arg Gly His Val Pro Trp Gly Leu Glu Glu Ile Leu Asp Val 1 5 10 15

Ile Glu Pro Ser Gln Phe Val Lys Ile Gln Glu Pro Leu Phe Lys Gln 20 25 30

Ile Ala Lys Cys Val Ser Ser Pro His Phe Gln Val Ala Glu Arg Ala
35 40 45

Leu Tyr Tyr Trp Asn Asn Glu Tyr Ile Met Ser Leu Ile Glu Glu Asn 50 60

Ser Asn Val Ile Leu Pro Ile Met Phe Ser Ser Leu Tyr Arg Ile Ser 65 70 75 80

Lys Glu His Trp Asn Pro Ala Ile Val Ala Leu Val Tyr Asn Val Leu
85 90 95

Lys Ala Phe Met Glu Met Asn Ser Thr Met Phe Asp Glu Leu Thr Ala 100 105 110

Thr Tyr Lys Ser Asp Arg Gln Arg Glu Lys Lys Glu Lys Glu Arg

Glu Glu Leu Trp Lys Lys Leu Glu Asp Leu Glu Leu Lys Arg Gly Leu 130 135 140

Arg Arg Asp Gly Ile Ile Pro Thr 145 150

<210> 901

<211> 261

<212> PRT

<213> Homo sapiens

<400> 901

Gly Leu Arg Glu Ile Ser Gly Arg Leu Ala Glu Met Pro Ala Asp Ser

WO 00/55350 PCT/US00/05882

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Gly	туг	Pro	Ala 20	Tyr	Leu	Gly	Ála	Arg 25	Leu	Ala	Ser	Phe	Tyr 30	Glu	Arg
Ala	Gly	Arg 35	Val	Lys	Cys	Leu	Gly 40	Asn	Pro	Glu	Arg	Glu 45	Gly	Ser	Val
Ser	Ile 50	.Val	Gly	Ala	Val	Ser 55	Pro	Pro	Gly	Gly	Asp 60	Phe	Ser	Asp	Pro
Val 65	Thr	Ser	Ala	Thr	Leu 70	Gly	Ile	Val	Gln	Val 75	Phe	Trp	Gly	Leu	Asp 80
Lys	Lys	Leu	Ala	Gln 85	Arg	Lys	His	Phe	Pro 90	Ser	val	Asn	Trp	Leu 95	Ile
Ser	Tyr.	Ser	Lys 100	Tyr	Met	Arg	Ala	Leu 105	Asp	Glu	Tyr	Tyr	Asp 110	Lys	His
Phe	Thr	Glu 115	Phe	Val	Pro	Leu	Arg 120	Thr	Lys	Ala	Lys	Glu 125	Ile	Leu	Gln
Glu	Glu 130	Glu	Asp	Leu	Ala	Glu 135	Ile	Val	Gln	Leu	Val 140	Gly	Lys	Ala	Ser
Leu 145	Ala	Glu	Thr	Asp	Lys 150	Ile	Thr	Leu	Glu	Val 155	Ala	Lys	Leu	Ile	Lys 160
Asp	Asp	Phe	Leu	Gln 165	Gln	Asn	Gly	Tyr	Thr 170	Pro	Tyr	Asp	Arg	Phe 175	Cys
Pro	Phe	туr	Lys 180	Thr	Val	Gly	Met	Leu 185	Ser	Asn	Met	Ile	Ala 190	Phe	Tyr
Asp	Met	Ala 195	Arg	Arg	Val	Phe	Glu 200	Thr	Thr	Ala	Gln	Ser 205	Asp	Asn	Lys
Ile	Thr 210	Trp	Ser	Ile	Ile	Arg 215	Glu	His	Met	Gly	Asp 220	Ile	Leu	Tyr	Lys
Leu 225	Ser	Ser	Met	Lys	Phe 230	Lys	Asp	Pro	Leu	Lys 235	Asp	Gly	Glu	Ala	Lys 240
Ile	Lys	Ser	Asp	Tyr 245	Ala	Gln	Leu	Leu	Glu 250	Asp	Met	Gln	Asn	Ala 255	Phe
Arg	Ser	Leu	Glu 260	Asp											

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<21	3> H	omo :	sapi	ens											
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		-	qual	s any	y of	the	nati	ural	ly o	ccur	ring	L-ai	nino	aci	ds
<40	0> 9	02													
Phe 1	Pro	Gly	Arg	Pro 5	Thr	Arg	Pro	Arg	Gly 10	Ile	Ser	Val	Ser	Gly 15	Gl
Gĺu	Ala	Val	Cys 20	Pro	Val	Gln	Trp	Arg 25	Leu	Arg	Lys	Leu	Ala 30	Ala	Al
Xaa	Gly	Lys 35	Gly	Gln	Glu	Val	Glu 40	Thr	Ser	Val	Thr	Tyr 45	туг	Arg	Le
Glu	Glu 50	Val	Ala	Lys	Arg	Asn 55	Ser	Leu	Lys	Glu	Leu 60	Trp	Leu	Val	11
His 65	Gly	Arg	Val	Tyr	Asp 70	Val	Thr	Arg	Phe	Leu 75	Asn	Glu	His	Pro	G1;
Gly	Glu	Glu	Val	Leu 85	Leu	Glu	Gln	Ala	Gly 90	Val	Asp	Ala	Ser	Glu 95	Se
Phe	Glu	Asp	Val 100	Gly	His	Ser	Ser	Asp 105	Ala	Arg	Glu	Met	Leu 110	Lys	Gl
туг	Tyr	Ile 115	Gly	Asp	Ile	His	Pro 120	Ser	Asp	Leu	Lys	Pro 125	Glu	Ser	Gl
Ser	Lys 130	Asp	Pro	Ser	Lys	Asn 135	Asp	Thr	Cys	Lys	Ser 140	Cys	Trp	Ala	ту
Trp	Ile	Leu	Pro	Ile	Ile	_	Ala	Val		Leu	Gly	Phe	Leu	_	Are

<210> 903

<211> 53

<212> PRT

<213> Homo sapiens

Tyr Tyr Thr Ser Glu Ser Lys Ser Ser

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<220>
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Pro Leu Cys Leu Ala Lys Asn Lys Asn Phe Leu Ile Leu Arg Xaa Asn
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Ile Gln Xaa Ile His Ile Lys Ser Leu Glu Asn Ile Ile Pro Phe Asp
                                 25
Ser Leu Ile Thr Leu Leu Glu Tyr Lys Glu Met Ile Leu Asn Ile Tyr
         35
                             40
Val Val Leu Trp Ser
     50
<210> 904
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<400> 904
Arg Arg Xaa Ala Xaa Pro Arg Val Arg Trp Lys Ile Cys Gly Leu Ser
                                     10
Pro Thr Thr Leu Ala Ile Tyr Phe Glu Val Val Asn Gln His Asn
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20 25 30 Ala Pro Ile Xaa Gln Gly Gly Arg Gly Ala Ile Gln Phe Val Thr Gln 40 Tyr Gln His Ser Ser Gly Gln Arg Arg Ile Arg Val Thr Thr Ile Ala Arg Asn Trp Ala Asp Ala Gln Thr Gln Ile Gln Asn Ile Ala Ala Ser Phe Asp Gln Glu Ala Ala Ala Ile Leu Met Ala Arg Leu Ala Ile Tyr 90 Arg Ala Glu Thr Glu Glu Gly Pro Asp Val Leu Arg Trp Leu Asp Arg Gln Leu Ile Arg Leu Cys Gln Lys Phe Gly Glu Tyr His Lys Asp Asp 120 Pro Ser Ser Phe Arg Phe Ser Glu Thr Phe Ser Leu Tyr Pro Gln Phe 135 Met Phe His Leu Arg Arg Ser Ser Phe Leu Gln Val Phe Asn Asn Ser 150 Pro Asp Glu Ser Ser Tyr Tyr Arg His His Phe Met Arg Gln Asp Leu 170 Thr Gln Ser Leu Ile Met Ile Gln Pro Ile Leu Tyr Ala Tyr Ser Phe 180 185 Ser Gly Pro Pro Glu Pro Val Leu Leu Asp Ser Ser Ser Ile Leu Ala 200 Asp Arg Ile Leu Leu Met Asp Thr Phe Phe Gln Ile Leu Ile Tyr His 210 215 Gly Glu Thr Ile Ala Gln Trp Arg Lys Ser Gly Tyr Gln Asp Met Pro 230 235 Glu Tyr Glu Asn Phe Arg His Leu Leu Gln Ala Pro Val Asp Asp Ala 250 Gln Glu Ile Leu His Ser Arg Phe Pro Met Pro Arg Tyr Ile Asp Thr 260 Glu His Gly Gly Ser Gln Ala Arg Phe Leu Leu Ser Lys Val Asn Pro 280

Ser Gln Thr His Asn Asn Met Tyr Ala Trp Gly Gln Glu Ser Gly Ala

290 295 300 Pro Ile Leu Thr Asp Asp Val Ser Leu Gln Val Phe Met Asp His Leu 310 315 Lys Lys Leu Ala Val Ser Ser Ala Ala 325 <210> 905 <211> 264 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (48) <223> Xaa equals any of the naturally occurring L-amino acids Phe Leu Leu Pro Thr Leu Trp Phe Cys Ser Pro Ser Ala Lys Tyr Phe 10 Phe Lys Met Ala Phe Tyr Asn Gly Trp Ile Leu Phe Leu Ala Val Leu 20 25 Ala Ile Pro Val Cys Ala Val Arg Gly Arg Asn Val Glu Asn Met Xaa 40 Ile Leu Arg Leu Met Leu Leu His Ile Lys Tyr Leu Tyr Gly Ile Arg 55 Val Glu Val Arg Gly Ala His His Phe Pro Pro Ser Gln Pro Tyr Val 65 70 75 Val Val Ser Asn His Gln Ser Ser Leu Asp Leu Leu Gly Met Met Glu 90 Val Leu Pro Gly Arg Cys Val Pro Ile Ala Lys Arg Glu Leu Leu Trp 105 Ala Gly Ser Ala Gly Leu Ala Cys Trp Leu Ala Gly Val Ile Phe Ile 115 Asp Arg Lys Arg Thr Gly Asp Ala Ile Ser Val Met Ser Glu Val Ala 135

Gln Thr Leu Leu Thr Gln Asp Val Arg Val Trp Val Phe Pro Glu Gly

Thr Arg Asn His Asn Gly Ser Met Leu Pro Phe Lys Arg Gly Ala Phe 165 170 175

His Leu Ala Val Gln Ala Gln Val Pro Ile Val Pro Ile Val Met Ser 180 185 190

Ser Tyr Gln Asp Phe Tyr Cys Lys Lys Glu Arg Arg Phe Thr Ser Gly 195 200 205

Gln Cys Gln Val Arg Val Leu Pro Pro Val Pro Thr Glu Gly Leu Thr 210 215 220

Pro Asp Asp Val Pro Ala Leu Ala Asp Arg Val Arg His Ser Met Leu 225 230 235 240

Thr Val Phe Arg Glu Ile Ser Thr Asp Gly Arg Gly Gly Gly Asp Tyr 245 250 255

Leu Lys Lys Pro Gly Gly Gly Gly 260

<210> 906

<211> 189

<212> PRT

<213> Homo sapiens

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>

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<222> (4)

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<400> 906

Xaa Xaa Pro Xaa Pro Glu Phe Pro Gly Arg Thr His Ala Ser Gly Leu
1 5 10 15

Leu Arg Ser Arg Leu Ala Leu Arg Trp Leu Ser His Val Arg Arg Pro 20 25 30

Ser Arg Arg Val Pro Arg Met Pro Arg Gly Ser Arg Ser Arg Thr Ser

<222> (52)

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35 45 Arg Met Ala Pro Pro Ala Ser Arg Ala Pro Gln Met Arg Ala Ala Pro 55 Arg Pro Ala Pro Val Ala Gln Pro Pro Ala Ala Pro Pro Ser Ala 70 65 Val Gly Ser Ser Ala Ala Ala Pro Arg Gln Pro Gly Leu Met Ala Gln Met Ala Thr Thr Ala Ala Gly Val Ala Val Gly Ser Ala Val Gly His 100 105 Thr Leu Gly His Ala Ile Thr Gly Gly Phe Ser Gly Gly Ser Asn Ala 115 120 Glu Pro Ala Arg Pro Asp Ile Thr Tyr Gln Glu Pro Gln Gly Thr Gln 135 Pro Ala Gln Gln Gln Pro Cys Leu Tyr Glu Ile Lys Gln Phe Leu 145 Glu Cys Ala Gln Asn Gln Gly Asp Ile Lys Leu Cys Glu Gly Phe Asn 170 Glu Val Leu Lys Gln Cys Arg Leu Ala Asn Gly Leu Ala 180 <210> 907 <211> 638 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (43) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE

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<223> Xaa equals any of the naturally occurring L-amino acids

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Tyr 1		Gln	Gly	Tyr 5		Leu	Ser	Gln	Ala 10	_	Val	Asp	Ala	Phe 15	Arg
Gln	Leu	Ser	Ala 20	Pro	Pro	Ala	Asp	Pro 25		Leu	Phe	His	Val 30	Ala	Arg
Trp	Phe	Arg 35	His	Ile	Glu	Ala	Leu 40	Leu	Gly	Xaa	Pro	Cys 45	Gly	Lys	Gly
Gln	Pro 50	Cys	Xaa	Leu	Pro	Ser 55	Xaa	Gln	Arg	Pro	Ala 60	Cys	Ala	Ala	Pro
Val 65	Val	Pro	Ser	Суз	Trp 70		Pro	Xaa	Cys	Arg 75	Leu	His	Leu	туг	Asn 80
Ser	Leu	Thr	Arg	Asn 85	Lys	Glu	Val	Phe	Ile 90	Pro	Gln	Asp	Gly	Lys 95	Lys
Val	Thr	Trp	Tyr 100	Cys	Cys	Gly	Pro	Thr 105	Val	Tyr	Asp	Ala	Ser 110	His	Met
Gly	His	Ala 115	Arg	Ser	Tyr	Ile	Ser 120	Phe	Asp	Ile	Leu	Arg 125	Arg	Val	Leu
Lys	Asp 130	Tyr	Phe	Lys	Phe	Asp 135	Val	Phe	Туr	Суз	Met 140	Asn	Ile	Thr	Asp
Ile 145	Asp	Asp	Lys	Ile	Ile 150	Lys	Arg	Ala	Arg	Gln 155	Asn	Hįs	Leu	Phe	Glu 160
Gln	Tyr	Arg	Glu	Lys 165	Arg	Pro	Glu	Ala	Ala 170	Gln	Leu	Leu	Glu	Asp 175	Val
Gln	Ala	Ala	Leu 180	Lys	Pro	Phe	Ser	Val 185	Lys	Leu	Asn	Glu	Thr 190	Thr	Asp
Pro	Asp	Lys 195	Lys	Gln	Met	Leu	Glu 200	Arg	Ile	Gln	His	Ala 205	Val	Gln	Leu
Ala	Thr	Glu	Pro	Leu	Glu	Lys	Ala	Val	Gln	Ser	Arg	Leu	Thr	Gly	Glu

	210					215					. 220				
Glu 225	Val	Asn	Ser	Cys	Val 230	Glu	Val	Leu	Leu	Glu 235	Glu	Ala	Lys	Asp	Leu 240
Leu	Ser	Asp	Trp	Leu 245	Asp	Ser	Thr	Leu	Gly 250	Cys	Asp	Val	Thr	Asp 255	Asn
Ser	Ile	Phe	Ser 260	Lys	Leu	Pro	Lys	Phe 265	Trp	Glu	Gly	Asp	Phe 270	His	Arg
Asp	Met	Glu 275	Ala	Leu	Asn	Val	Leu 280	Pro	Pro	Asp	Val	Leu 285	Thr	Arg	Val
Ser	Glu 290	Tyr	Val	Pro	Glu	Ile 295	Val	Asn	Phe	Val	Gln 300	Lys	Ile	Val	Asp
Asn 305	Gly	Tyr	Gly	Tyr	Val 310	Ser	Asn	Gly	Ser	Val 315	Tyr	Phe	Asp	Thr	Ala 320
Lys	Phe	Ala	Ser	Ser 325	Glu	Lys	His	Ser	Туг 330	Gly	Lys	Leu	Val	Pro 335	Glu
Ala	Val	Gly	Asp 340	Gln	Lys	Ala	Leu	Gln 345	Glu	Gly	Glu	Gly	Asp 350	Leu	Ser
Ile	Ser	Ala 355	Asp	Arg	Leu	Ser	Glu 360	Lys	Arg	Ser	Pro	Asn 365	Asp	Phe	Ala
Leu	Trp 370	Lys	Ala	Ser	Lys	Pro 375	Gly	Glu	Pro	Ser	Trp 380	Pro	Cys	Pro	Trp
Gly 385	Lys	Gly	Arg	Pro	Gly 390	Trp	His	Ile	Glu	Cys 395	Ser	Ala	Met	Ala	Gly 400
Thr	Leu	Leu	Gly	Ala 405	Ser	Met	Asp	Ile	His 410	Gly	Gly	Gly	Phe	Asp 415	Leu
Arg	Phe	Pro	His 420	His	Asp	Asn	Glu	Leu 425	Ala	Xaa	Ser	Glu	Ala 430	Tyr	Phe
Glu	Asn	Asp 435	Cys	Trp	Val	Arg	Tyr 440	Phe	Leu	His	Thr	Gly 445	His	Leu	Thr
Ile	Ala 450	Gly	Cys	Lys	Met	Ser 455	Lys	Ser	Leu	Lys	Asn 460	Phe	Ile	Thr	Ile
Lys 465	Asp	Ala	Leu	Lys	Lys 470	His	Ser	Ala	Arg	Gln 475	Leu	Arg	Leu	Ala	Phe 480
Leu	Met	His	Ser	Trp	Lys	Asp	Thr	Leu	Asp	Tyr	Ser	Ser	Asn	Thr	Met

Glu	Ser	Ala	Leu 500	Gln	туг	Glu	Lys	Phe 505		Asn	Glu	Phe	Phe 510	Leu	Asn
Val	Lys	Asp 515	Ile	Leu	Arg	Ala	Pro 520	Val	Asp	Ile	Thr	Gly 525	Gln	Phe	Glu
Lys	Trp 530	Gly	Glu	Glu	Glu	Ala 535	Glu	Leu	Asn	Lys	Asn 540	Phe	Tyr	Asp	Lys
Lys 545	Thr	Ala	Ile	His	Lys 550	Ala	Leu	Cys	Asp	Asn 555	Val	Asp	Thr	Arg	Thr 560
Val	Met	Glu	Glu	Met 565	Arg	Ala	Leu	Val	Ser 570	Gln	Cys	Asn	Leu	Tyr 575	Met
Ala	Ala	Arg	Lys 580	Ala	Val	Arg	Lys	Arg 585	Pro	Asn	Gln	Ala	Leu 590	Leu	Glu
Asn	Ile	Ala 595	Leu	Tyr	Leu	Thr	His 600	Met	Leu	Lys	Ile	Phe 605	Gly	Ala	Val
Glu	Glu 610	Asp	Ser	Ser	Leu	Gly 615	Phe	Pro	Val	Gly	Gly 620	Pro	Gly	Thr	Ser
Leu 625	Ser	Leu	Glu	Ala	Thr 630	Val	Met	Pro	туг	Leu 635	Gln	Val	Leu		
<211 <212)> 9(.> 24 !> PF !> Ho	18	apie	ens				-							
<400	> 90	18													
			Leu	Arg 5	Ser	Arg	Leu ,	Pro	Ser 10	Ala	Thr	Gly	Val	Gly 15	His
Ala	Leu	Ala	Arg 20	Ser	Phe	Cys	Arg	His 25	Leu	Gly	Ser	Ala	Phe 30	Pro	Ala
Gln	Asn	Ala 35	Arg	Arg	Ser	Thr	Glu 40	Thr	Val	Pro	Ala	Thr 45	Glu	Gln	Glu
Leu	Pro 50	Gln	Pro	Gln	Ala	Glu 55	Thr	Gly	Ser	Gly	Thr 60	Glu	Ser	Asp	Ser
Asp 65	Glu	Ser	Val	Pro	Glu 70	Leu	Glu	Glu	Gln	Asp 75	Ser	Thr	Gln	Ala	Thr 80

Thr Gln Gln Ala Gln Leu Ala Ala Ala Glu Ile Asp Glu Glu Pro
85 90 95

Val Ser Lys Ala Lys Gln Ser Arg Ser Glu Lys Lys Ala Arg Lys Ala 100 105 110

Met Ser Lys Leu Gly Leu Arg Gln Val Thr Gly Val Thr Arg Val Thr 115 120 125

Ile Arg Lys Ser Lys Asn Ile Leu Phe Val Ile Thr Lys Pro Asp Val 130 135 140

Tyr Lys Ser Pro Ala Ser Asp Thr Tyr Ile Val Phe Gly Glu Ala Lys 145 150 155 160

Ile Glu Asp Leu Ser Gln Gln Ala Gln Leu Ala Ala Glu Lys Phe 165 170 175

Lys Val Gln Gly Glu Ala Val Ser Asn Ile Gln Glu Asn Thr Gln Thr 180 185 . 190

Pro Thr Val Gln Glu Glu Ser Glu Glu Glu Glu Val Asp Glu Thr Gly 195 200 205

Val Glu Val Lys Asp Ile Glu Leu Val Met Ser Gln Ala Asn Val Ser 210. 215 220

Arg Ala Lys Ala Val Arg Ala Leu Lys Asn Asn Ser Asn Asp Ile Val 225 230 235 240

Asn Ala Ile Met Glu Leu Thr Met 245

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<213> Homo sapiens

<220>

<221> SITE

<222> (46)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (158)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 909 Gln Gly Cys Cys Tyr Gly Ala Gly Arg Arg Val Ala Arg Leu Leu Ala 10 Pro Leu Met Trp Arg Ala Val Ser Ser Val Ala Gly Ser Ala Val 25 Gly Ala Glu Pro Gly Leu Arg Leu Leu Ala Val Gln Arg Xaa Pro Val Glu Gln Arg Ser Ala Gly Leu Ala Arg Pro Gln Thr Leu Ser Ala Ala Cys Thr Ala Lys Pro Gly Leu Glu Glu Arg Ala Glu Gly Thr Val Asn 70 Glu Gly Arg Pro Glu Ser Asp Ala Ala Asp His Thr Gly Pro Lys Phe 90 Asp Ile Asp Met Met Val Ser Leu Leu Arg Gln Glu Asn Ala Arg Asp 105 Ile Cys Val Ile Gln Val Pro Pro Glu Met Arg Tyr Thr Asp Tyr Phe 115 120 Val Ile Val Ser Gly Thr Ser Thr Arg His Leu His Ala Met Ala Phe 135 Tyr Val Val Lys Met Tyr Lys His Leu Lys Cys Lys Arg Xaa Pro Ser 155 150 Cys

<210> 910

<211> 487

<212> PRT

<213> Homo sapiens

<400> 910

Lys Ala Ala Ser Gly Pro Ala Thr Ser Ile Thr Gly Val Thr Met Gly
1 5 10 15

Ala Val Leu Gly Val Phe Ser Leu Ala Ser Trp Val Pro Cys Leu Cys
20 25 30

Ser Gly Ala Ser Cys Leu Leu Cys Ser Cys Cys Pro Asn Ser Lys Asn

Ser	Thr 50		Thr	Arg	Leu	Ile 55	-	Ala	Phe	Ile	Leu 60		Leu	Ser	Thr
Val 65		Ser	Tyr	Ile	Met 70	Gln	Arg	Lys	Glu	Met 75	Glu	Thr	Tyr	Leu	Lys 80
Lys	Ile	Pro	Gly	Phe 85	_	Glu	Gly	Gly	Phe 90	_	Ile	His	Glu	Ala 95	-
Ile	Asn	Ala	Asp 100	Lys	Asp	Cys	Asp	Val 105	Leu	Val	Gly	Tyr	Lys 110	Ala	Val
Tyr	Arg	Ile 115	Ser	Phe	Ala	Met	Ala 120	Ile	Phe	Phe	Phe	Val 125	Phe	Ser	Leu
Leu	Met 130	Phe	Lys	Val	Lys	Thr 135	Ser	Lys	Asp	Leu	Arg 140	Ala	Ala	Val	His
Asn 145	Gly	Phe	Trp	Phe	Phe 150	Lys	Ile	Ala	Ala	Leu 155	Ile	Gly	Ile	Met	Val 160
				165					170		Ser		_	175	
			180					185			Ile		190		
		195					200				Trp	205			
	210	_				215	_	_			Leu 220				
225			,		230					235	Gly			-	240
				245					250		Lys			255	
			260					265	,		Ile		270		
		275					280		_		Leu	285			
	290					295					Ala 300				
Pro 305	Asp	Arg	Ser	Cys	Asn 310	Pro	Asn	Leu	Met	Ser 315	Phe	Ile	Thr	Arg	11e 320